



**INMED PHARMACEUTICALS INC.**

**Annual Information Form  
For the year ended June 30, 2018**

**September 13, 2018**

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## MEANINGS OF CERTAIN REFERENCES

In this annual information form, or AIF, references to the “Company”, “InMed”, “we”, “us” or “its” are references to InMed Pharmaceutical Inc. References to “management” in this AIF mean the persons acting in the capacities of InMed’s President and Chief Executive Officer, Chief Financial Officer, Chief Business Officer, Chief Scientific Officer, Senior Vice President – Clinical and Regulatory Affairs and Vice President – Preclinical Research and Development. Any statements in this AIF made by or on behalf of management are made in such persons’ capacities as officers of InMed and not in their personal capacities.

## FORWARD-LOOKING STATEMENTS

Certain statements in this AIF may constitute “forward-looking information” or “forward-looking statements” within the meaning of applicable securities laws (collectively, “forward-looking statements”). These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements or industry results to be materially different from any future results, performance or achievements or industry results expressed or implied by such forward-looking information or financial outlook. Forward-looking statements are identified by the use of terms and phrases such as “anticipate”, “believe”, “could”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “will”, “would”, and similar terms and phrases, including references to assumptions. Such information may involve, but is not limited to, comments with respect to strategies, expectations, planned operations or future actions. Forward-looking statements in this AIF include, without limitation, statements with respect to: initiating discussions with potential partners for the development of an ocular delivery system; our ability to successfully build a dedicated cannabinoid biosynthesis facility or to transfer our biosynthesis process for manufacturing to a contract manufacturing organization with existing infrastructure to produce for us the preclinical, clinical and commercial scale supply of our product candidates; believing that the biosynthesis manufacturing approach InMed is developing is robust and effective and will result in high-yields of cannabinoids; believing that the biosynthesis manufacturing approach InMed is developing and products produced using it face less obstacles when it comes to regulatory approval than products produced via traditional plant growing, harvesting, processing, extraction and purification techniques; believing that additional pre-clinical pharmacology experiments for INM-750 will help the Company better understand the contributions of each cannabinoid component as well as their final combination in INM-750; believing that INM-750 offers specific advantages and will prove to provide the most extensive relief symptomology with the added potential of addressing the underlying disease in EB; anticipating that InMed’s biosynthesis program will have been successfully scaled up so that it will be commercial-scale ready after Phase 1 and Phase 2a clinical trials are completed, after which time InMed will no longer need to source APIs from contract manufacturers; the key next steps in InMed’s biosynthesis program, including continuing efforts to diversify the number of cannabinoids produced, scaling-up the biosynthesis process to larger vessels and identifying external vendors to assist in the commercial scale-up of the process; optimizing fermentation conditions and downstream purification processes with yet-to-be announced 3rd party suppliers; making determinations as to which R&D programs to continue based on several strategic factors; looking to license or sell certain new drug candidates to pharmaceutical companies for further development, commercialization and distribution; the possibility of InMed entering into service/license agreements for access to its bioinformatics platform, and the expectation that such agreements, if entered into, would provide only very limited revenues until a commercial product results from such agreements with no significant revenues from such licenses expected for several years; taking an opportunistic approach in this rapidly emerging sector of pharmaceutical development to maximize the return to investors/shareholders; continuing to outsource the majority of the Company’s research and development activities through scientific collaboration agreements and fee for service arrangements with various scientific collaborators, academic institutions and their personnel; the work to be conducted under the research and development collaboration between the Company and ATERA SAS and Fraunhofer Institute; the work to be conducted under the research and development agreement between the Company and Pharmaseed Ltd.; developing our therapies through early human testing, and then evaluating the financial returns on a ‘go-it-alone’ commercialization effort versus out-licensing to third parties, who would continue to advance human testing, seek regulatory approval, and subsequent product sales and marketing; relying on licensing and/or co-promotion agreements with strategic collaborators for the commercialization of our products in the United States and other territories; overseeing clinical trials for INM-750 in EB and building the requisite internal commercialization infrastructure to self-market the product to EB clinics; seeking a partnership early in the development process for INM-085 in glaucoma; the estimate that glaucoma will reach a global prevalence of 80 million people by 2020; the estimate that osteoarthritis is expected to impact over 130

million individuals worldwide by 2050; utilizing the bioinformatics platform to identify internal drug candidates for diseases / segments of strategic interest to InMed and its drug development programs; utilizing the bioinformatics platform for the discovery process to generate further intellectual property for the Company; out-licensing drug candidates to third parties in those areas of low strategic interest to InMed in order to maximize revenue potential, potentially leading to drug supply agreements using our biosynthesis program; intending to potentially earn revenue from our biosynthesis program by (i) becoming a supplier of drug product to the pharmaceutical industry, (ii) providing raw material to the flavors and fragrance market, and (iii) providing pharmaceutical-grade ingredients to the legal cannabis market; introducing a revenue stream to the Company well before the expected commercial approval of our therapeutic programs; increase value to our shareholders by extending overall valuation opportunities for the underlying Company; planning preliminary meetings with regulatory authorities for INM-750 for the first half of calendar year 2019 to include data on formulation development and advanced preclinical toxicology studies; expecting to file an Investigational New Drug application for INM-750 in the second half of calendar year 2019; planning to work closely with regulatory authorities and clinical experts in developing the clinical program for INM-750; the eligibility of EB for a Rare Pediatric Disease Priority Review Voucher; INM-085 being a once-a-day eye drop medication that will compete with treatment modalities in the ‘medicines’ category; developing a stimulus-responsive, nanoparticle-laden hydrogel vehicle for spatiotemporal and dosage-controlled release of cannabinoids into the aqueous humor of the eye, packaged as a liquid and intended for application as a once-per-day eye drop administered immediately prior to the patient’s bedtime; the potential of INM-085 to assist in reducing the high rate of non-adherence with current glaucoma therapies; the first applications of InMed’s stimulus-responsive, nanoparticle-laden vehicle for controlled delivery of ophthalmic drugs being for INM-085; believing that with a novel delivery system, the reduction of IOP in glaucoma patients by topical (eye drop) application of cannabinoids will hold significant promise as a new therapy; the expectation that the results from InMed’s *in vitro* studies using surrogate biomarkers will form part of a new patent application for the treatment of glaucoma; the potential of peripheral application of certain cannabinoid compounds, alone or in combination, such as INM-405 to be effective in the treatment of craniofacial muscle pain disorders, without any observed CNS side effects, and for them to be a more desirable strategy than systemic pain-relief administration; the patient populations for the clinical pathway for INM-405 being comparatively limited or very extensive, depending on the target indication; the potential to out-license InMed’s delivery vehicle to other companies with ophthalmic drugs; the ability to re-invigorate the commercial potential of off-patent products with InMed’s ocular delivery vehicle; InMed’s intention to utilize the full complement of patents available to protect its intellectual property; the potential for any of InMed’s patent applications to provide intellectual property protection for InMed; intending to not file for patent protection for our bioinformatics platform but to instead protect this asset as internal know-how; expecting that the final formulations of both the INM-750 topical product and the INM-085 eye drop formulation will be manufactured by contract manufacturers and sub-component fabricators; securing insurance coverage for shipping and storage of product candidates, and clinical trial insurance; expanding our insurance coverage to include the commercial sale of approved drug products; InMed’s expectation that its funds available as at June 30, 2018 will be sufficient to funds its operations for the next 24 months which will include a significant increase in R&D spending; continuing investment in each of InMed’s non-core asset programs; choosing to partner some or all non-core asset programs with external parties; initiating discussions with potential partners; positioning the Company to achieve value-driving, near-term milestones for its product candidates with limited investment; the Company’s ability to execute its business strategy; critical accounting estimates; management’s assessment of future plans and operations; the outlook of the Company’s business and the global economic and geopolitical conditions; the competitive environment in which the Company and its business units operate; and declaring dividends. Actual events or results may differ materially.

The forecasts and projections that make up the forward-looking statements in this AIF are based on assumptions which include, but are not limited to: additional financing being available; InMed’s clinical development is not stalled; there are no material exchange rate fluctuations between the Canadian and U.S. Dollar that affect InMed’s performance; the general state of the economy does not worsen; InMed does not lose any key personnel; InMed is able to grow its business long term and to manage its growth; InMed is able to comply with existing regulations and will not become subject to more stringent regulations; no material product liability claims; InMed successfully completing its various patent applications; InMed successfully protecting its intellectual property; InMed’s management information systems upon which it is dependent are not impaired; InMed’s insurance is sufficient to cover losses that may occur as a result of its operations; there are no changes to tax laws other than the specific amendments, in their currently proposed form, which are already known; the availability of resources and our ability to find funding partners; and applicable laws not being changed in a manner that is unfavourable to InMed.

The forward-looking statements in this AIF are subject to risks, uncertainties and other factors that could cause actual results to differ materially from historical results or results anticipated by the forward-looking statements. The factors which could cause results to differ from current expectations include, but are not limited to: InMed may not be able to obtain debt or equity financing necessary to support the growth of the Company; import/export and research restrictions for cannabinoid-based pharmaceuticals may delay or prevent the development of InMed's products in various geographical jurisdictions; InMed's products may not gain regulatory approval on a timely basis, or at all; InMed may not be able to protect its intellectual property; clinical development may not proceed as intended, or at all; exchange rate fluctuations between the Canadian and U.S. Dollar could affect InMed's performance; InMed's results are dependent upon the general state of the economy; InMed depends on key personnel, the loss of which could harm its business; InMed may be unable to grow its business long term or to manage any growth; InMed may fail to comply with existing regulations or become subject to more stringent regulations; InMed is dependent upon its management information systems; InMed's insurance may be insufficient to cover losses that may occur as a result of InMed's operations; the market price of the Common Shares and Listed Warrants will fluctuate; there is a possibility of dilution of existing Shareholders; InMed may suffer a cyber-security breach; applicable laws may change unfavourably; InMed may cease to invest in its non-core assets; and relevant public perception may change unfavourably. For additional information with respect to risks and uncertainties, readers should carefully review and consider the risk factors described under the section "*Risk Factors*" and elsewhere in this AIF. The information contained in this AIF identifies additional factors that could affect the operating results and performance of InMed. Shareholders and prospective investors are urged to carefully consider those factors.

Readers are cautioned that the preparation of financial statements in accordance with IFRS requires management of InMed to make certain judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses.

The forward-looking statements contained herein are expressly qualified in their entirety by this cautionary statement. Forward-looking statements reflect management's current beliefs and are based on information currently available to InMed. The forward-looking statements are made as of the date of this AIF (or in the case of information contained in a document incorporated by reference herein, as of the date of such document), and InMed assumes no obligation to publicly update or revise such forward-looking information to reflect new information, subsequent or otherwise, except as may be required by applicable securities law.

#### **DATE OF INFORMATION**

The information in this AIF is presented as of June 30, 2018, unless otherwise indicated.

#### **PRESENTATION OF FINANCIAL INFORMATION**

Unless otherwise indicated, all references to "\$" or "dollars" are to Canadian dollars, which is InMed's functional currency. The fiscal year end of all entities within the corporate structure of InMed is June 30. InMed's financial statements are prepared in accordance with IFRS.

#### **THIRD PARTY INFORMATION**

This AIF includes industry and market data and forecasts obtained from independent publications, market research and analyst reports, surveys and other publicly available sources. Although InMed believes these sources to be generally reliable, market and industry data is subject to interpretation and cannot be verified with complete certainty due to limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties inherent in any statistical survey. Accordingly, the accuracy and completeness of this data is not guaranteed. InMed has not independently verified any of the data from third party sources referred to in this AIF nor ascertained the underlying assumptions relied upon by such sources.

## CORPORATE STRUCTURE

### **InMed Pharmaceuticals Inc.**

InMed was incorporated on May 19, 1981 under the *Company Act* (British Columbia), which legislation has since been repealed and replaced by the *Business Corporations Act* (British Columbia), under the name Kadrey Energy Corporation. InMed has undergone a number of corporate name changes since its incorporation, most recently changing its name from Cannabis Technologies Inc. to InMed Pharmaceuticals Inc. on October 6, 2014. InMed's head office is located at Suite 340 – 200 Granville Street, Vancouver, British Columbia V6C 1S4 and its registered office is located at 2500-700 West Georgia Street, Vancouver, British Columbia V7Y 1B3.

The common shares in the capital of the Company (the “Common Shares”) are listed on the Toronto Stock Exchange (“TSX”) under the trading symbol “IN”, and under the trading symbol “IMLFF” on the OTCQX® Best Market. Prior to March 26, 2018, the Company's shares were listed on the Canadian Securities Exchange (“CSE”). Prior to May 4, 2018, the Company's shares traded on the OTCQB® Venture Market. In addition, common share purchase warrants issued by the Company on June 21, 2018 (the “Listed Warrants”) are listed on the TSX under the trading symbol “IN.WT”. More information can be found below under “*Capital Structure*”.

On March 24, 2017, InMed held a special meeting of its shareholders at which InMed's shareholders approved, among other things, the amendment and restatement of the articles of InMed and the alteration of InMed's authorized share structure to cancel the Class A Preference Shares and Class B Preference Shares of InMed and to create an unlimited number of preferred shares without par value. InMed's amended and restated articles have been filed under InMed's profile on the system for electronic document analysis and retrieval, or SEDAR, at [www.sedar.com](http://www.sedar.com). These amendments to InMed's articles and its authorized share structure are summarized under the headings “Proposal 3 – Approval of Alteration to Share Structure” and “Proposal 4 – Approval of Alterations to Articles” in InMed's management information circular dated February 22, 2017, which disclosure is specifically incorporated by reference herein. A copy of the information circular for the 2017 special meeting has been filed under InMed's profile on SEDAR at [www.sedar.com](http://www.sedar.com).

### **Biogen Sciences Inc.**

Biogen Sciences Inc. was acquired by InMed on May 21, 2014. Biogen Sciences Inc. was incorporated on March 27, 2014 under the *Business Corporations Act* (British Columbia). Biogen Sciences Inc.'s head and registered office is located at 2500-700 West Georgia Street, Vancouver, British Columbia V7Y 1B3. All of the assets and liabilities of Biogen Sciences Inc. have been transferred to InMed. Accordingly, Biogen Sciences Inc. is currently inactive and has no material assets or liabilities.

InMed also wholly-owns each of Meridex Network Corporation (a British Columbia corporation, which has been statutorily dissolved), Savicon Inc. (an Idaho corporation, which has been administratively dissolved), Meridex USA (a Nevada corporation, which has been statutorily dissolved) and Sweetnam Consulting Inc. (an Ontario corporation). These subsidiaries of InMed are all currently inactive and have no material assets or liabilities.

## RISK FACTORS

Investing in InMed's securities involves a high degree of risk. In addition to the other information contained in this AIF, you should carefully consider the following risk factors before purchasing any securities of InMed, including its Common Shares and Listed Warrants. The occurrence of any of the following risks could materially and adversely affect InMed's investments, prospects, cash flows, results of operations or financial condition. In that event, the value of InMed's Common Shares and Listed Warrants and any other securities it may have issued and outstanding from time to time could decline and investors may lose all or part of their investment. Although InMed believes that the risk factors described below are the most material risks that InMed faces, they are not the only ones. Additional risk factors not presently known to InMed or that InMed currently believes are immaterial could also materially and adversely affect InMed's investments, prospects, cash flows, results of operations or financial condition and negatively affect the value of the Common Shares and Listed Warrants and any other securities of InMed that may be outstanding from time to time.

## **Risks Relating to InMed and its Business**

***The Company's financial statements for the year ended June 30, 2018 show recurring operating losses and negative cash flows which may have an adverse effect on its relationships with current and future collaborators, contract suppliers and investors.***

Since its inception, the Company has experienced recurring operating losses and negative cash flows and expects to continue to generate operating losses and consume significant cash resources for the foreseeable future. At June 30, 2018, the Company had a net working capital surplus of \$25,795,983 compared to a working capital surplus of \$6,574,847 at its previous fiscal year end of June 30, 2017. For the year ended June 30, 2018, the Company reported a loss of \$8,520,920 (2017 - \$4,473,849) and a cash outflow from operating activities of \$4,672,117 (2017 - \$3,076,396). As at June 30, 2018, the Company had an accumulated deficit of \$51,315,072 (June 30, 2017 - \$42,794,152).

Based on the funds available as at June 30, 2018, the Company estimates that it has cash resources for approximately the next 24 months which will fund a significant increase in R&D spend to continue development of its drug product candidates, including the preclinical and early clinical program for INM-750, the compilation of sufficient data for INM-085 to initiate the search for a development/commercialization partner, and further scale-up of the biosynthesis program, among other R&D activities. In order to continue operations beyond that time horizon, the Company will need to raise additional funds. There is no assurance that the Company will be successful in these efforts.

Any doubt about the Company's ability to continue as a going concern may materially and adversely affect the price the Company's Common Shares and Listed Warrants, and it may be more difficult for the Company to obtain financing. Any doubt about the Company's ability to continue as a going concern may also adversely affect the Company's relationships with current and future collaborators, contract manufacturers and investors, who may become concerned about its ability to meet its ongoing financial obligations. If potential collaborators decline to do business with the Company or potential investors decline to participate in any future financings due to such concerns, the Company's ability to increase its financial resources may be limited. The Company has prepared its financial statements on a going concern basis, which assumes that the Company will be able to meet its commitments, realize its assets and discharge its liabilities in the normal course of business. The Company's consolidated financial statements do not include any adjustment to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

***Our prospects depend on the success of our product candidates and technologies which are at early stages of development, and we do not expect to generate revenue for several years, if at all, from these products and technologies.***

Given the early stage of our product development, we can make no assurance that our research and development programs will result in regulatory approval or commercially viable products or technologies such as InMed's biosynthesis program. To achieve profitable operations, we, alone or with others, must successfully develop, gain regulatory approval, and market our future products. We currently have no products that have been approved by the United States Food and Drug Administration ('FDA'), Health Canada, or any similar regulatory authority. To obtain regulatory approvals for our product candidates being developed and to achieve commercial success, clinical trials must demonstrate that the product candidates are safe for human use and that they demonstrate efficacy. We have no products or technologies which are currently in human clinical trials. Additionally, we have no products for commercial sale or licensed for commercial sale, nor do we expect to have any such products for the next several years. Our only current potential source of revenue is licensing agreements for access to our bioinformatics platform. Such licensing agreements, if entered into, would provide only very limited revenues until a commercial product results from such agreement; significant revenues from such licenses are not expected for several years. As a result, we are not currently generating revenue from our products or technologies and do not expect to generate significant revenue from our products or technologies over the next several years and may never generate revenue from the sale or licensing of our products, or otherwise.

Many product candidates never reach the stage of clinical testing and even those that do have only a small chance of successfully completing clinical development and gaining regulatory approval. Product candidates may fail for a

number of reasons, including, but not limited to, being unsafe for human use or due to the failure to provide therapeutic benefits equal to or better than the standard of treatment at the time of testing. Positive results of early preclinical research may not be indicative of the results that will be obtained in later stages of preclinical or clinical research. Similarly, positive results from early stage clinical trials may not be indicative of favorable outcomes in later-stage clinical trials. We can make no assurance that any future studies, if undertaken, will yield favorable results. The early stage of our product development makes it particularly uncertain whether any of our product development efforts will prove to be successful and meet applicable regulatory requirements, and whether any of our product candidates will receive the requisite regulatory approvals, be capable of being manufactured at a reasonable cost or be successfully marketed. If we are successful in developing our current and future product candidates into approved products, we will still experience many potential obstacles such as the need to develop or obtain manufacturing, marketing and distribution capabilities. If we are unable to successfully commercialize any of our products, our financial condition and results of operations may be materially and adversely affected.

***If we have difficulty enrolling patients in clinical trials, the completion of the trials may be delayed or cancelled.***

As our product candidates advance from preclinical testing to clinical testing, and then through progressively larger and more complex clinical trials, we will need to enroll an increasing number of patients that meet our eligibility criteria. The factors that affect our ability to enroll patients are 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.

As a result of the foregoing factors, we may have difficulty enrolling or maintaining the enrollment of patients in any clinical trials conducted for our products, which may result in the delay or cancellation of such trials. The delay or cancellation of any clinical trials could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before us, which would impair our ability to successfully commercialize our product candidates and may harm our financial condition, results of operations and prospects.

***We rely on contract manufacturers over whom we have limited control. If we are subject to quality, cost or delivery issues with the preclinical and clinical grade materials supplied by contract manufacturers, our business operations could suffer significant harm.***

We currently have no manufacturing capabilities and rely on contract manufacturing organizations, or CMOs, to manufacture our product candidates for preclinical studies and clinical trials. We rely on CMOs for manufacturing, filling, packaging, storing and shipping of drug products in compliance with current good manufacturing practice, or cGMP, regulations applicable to our products. The FDA ensures the quality of drug products by carefully monitoring drug manufacturers' compliance with cGMP regulations. The cGMP regulations for drugs contain minimum requirements for the methods, facilities and controls used in manufacturing, processing and packing of a drug product. If our CMOs increase their prices or fail to meet our quality standards, or those of regulatory agencies such as the FDA, and cannot be replaced by other acceptable CMOs, our ability to obtain regulatory approval for and commercialize our product candidates may be materially adversely affected.

The active pharmaceutical ingredients, or APIs, used in INM-750, INM-085 and INM-405 are currently sourced from either contract manufacturers or, for smaller quantities, from research material suppliers, that utilize either synthetic chemistry or extraction techniques from plant-based sources. This is intended to be an interim step to enable InMed to proceed with developing its formulation, execute preclinical toxicology studies and progress through Phase 1 and 2a clinical trials, after which time we anticipate that we will have been able to successfully scale up InMed's

biosynthesis program so that it will be commercial-scale ready. Bridging studies consisting of chemical analysis and, possibly, animal studies may be required in order to switch our API from the current external manufacturing sources to our internal biosynthesized products. There is no guarantee that we will be successful in scaling up our biosynthesis manufacturing process for cannabinoids, or successfully complete any required bridging studies, or be able to successfully transfer our biosynthesis manufacturing process to a CMO. Failing to do this may mean that we are not able to produce certain cannabinoids in our product candidates in a cost effective manner. This could result in us not being able to successfully commercialize our product candidates, if any, that obtain regulatory approval.

***If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we would incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.***

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct preclinical studies in animals and extensive clinical trials in humans to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive and difficult to design and implement, can take many years to complete and has uncertain outcomes. The outcome of preclinical studies and early clinical trials may not predict the success of later clinical trials and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials. We do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any of our product candidates in any jurisdiction. A product candidate may fail for safety or efficacy reasons at any stage of the testing process. A major risk we face is the possibility that none of our product candidates under development will successfully gain market approval from the FDA or other regulatory authorities, resulting in us being unable to derive any commercial revenue from them after investing significant amounts of capital in multiple stages of preclinical and clinical testing. In addition, the eligibility of the EB indication for a Rare Pediatric Disease Priority Review Voucher is uncertain at this time. If it is not eligible, this may have a negative impact on our business.

***If we experience delays in clinical testing, we will be delayed in commercializing our product candidates, and our business may be substantially harmed.***

We cannot predict whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before us, which would impair our ability to successfully commercialize our product candidates and may harm our financial condition, results of operations and prospects. The commencement and completion of clinical trials for our products may be delayed for a number of reasons, including delays related, but not limited, to:

- failure by regulatory authorities to grant permission to proceed or placing the clinical trial on hold;
- import/export and research restrictions for cannabinoid-based pharmaceuticals may delay or prevent clinical trials in various geographical jurisdictions;
- patients failing to enroll or remain in our trials at the rate we expect;
- suspension or termination of clinical trials by regulators for many reasons, including concerns about patient safety or failure of our contract manufacturers to comply with cGMP requirements;
- any changes to our manufacturing process that may be necessary or desired;
- delays or failure to obtain clinical supply from contract manufacturers of our products necessary to conduct clinical trials;
- product candidates demonstrating a lack of safety or efficacy during clinical trials;
- patients choosing an alternative treatment for the indications for which we are developing any of our product candidates or participating in competing clinical trials and/or scheduling conflicts with participating clinicians;
- patients failing to complete clinical trials due to dissatisfaction with the treatment, side effects or other reasons;

- reports of clinical testing on similar technologies and products raising safety and/or efficacy concerns;
- clinical investigators not performing our clinical trials on their anticipated schedule, dropping out of a trial, or employing methods not consistent with the clinical trial protocol, regulatory requirements or other third parties not performing data collection and analysis in a timely or accurate manner;
- failure of our contract research organizations, or CROs, to satisfy their contractual duties or meet expected deadlines;
- inspections of clinical trial sites by regulatory authorities or Institutional Review Boards, or IRBs, or ethics committees finding regulatory violations that require us to undertake corrective action, resulting in suspension or termination of one or more sites or the imposition of a clinical hold on the entire study;
- one or more IRBs or ethics committees rejecting, suspending or terminating the study at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial; or
- failure to reach agreement on acceptable terms with prospective clinical trial sites.

Our product development costs will increase if we experience delays in testing or approval or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend study protocols to reflect these changes. Amendments may require us to resubmit our study protocols to regulatory authorities or IRBs or ethics committees for re-examination, which may impact the cost, timing or successful completion of that trial. Delays or increased product development costs may have a material adverse effect on our business, financial condition and prospects.

***Negative results from clinical trials or studies of others and adverse safety events involving the targets of our products may have an adverse impact on our future commercialization efforts.***

From time to time, studies or clinical trials on various aspects of biopharmaceutical products are conducted by academic researchers, competitors or others. The results of these studies or trials, when published, may have a significant effect on the market for the biopharmaceutical product that is the subject of the study. The publication of negative results of studies or clinical trials or adverse safety events related to our product candidates, or the therapeutic areas in which our product candidates compete, could adversely affect the price of our Common Shares and our ability to finance future development of our product candidates, and our business and financial results could be materially and adversely affected.

***We expect to face intense competition, often from companies with greater resources and experience than we have.***

The pharmaceutical industry is highly competitive and subject to rapid change. The industry continues to expand and evolve as an increasing number of competitors and potential competitors enter the market. Many of these competitors and potential competitors have substantially greater financial, technological, managerial and research and development resources and experience than we have. Some of these competitors and potential competitors have more experience than we have in the development of pharmaceutical products, including validation procedures and regulatory matters. Other companies researching in the same disease areas may develop products that are competitive or superior to our product candidates. Other companies working in cannabinoid research may develop products targeting the same diseases that we are focused on that are competitive or superior to our product candidates. In addition, there are non-FDA approved cannabis/cannabinoid preparations being made available from companies in the medical marijuana industry, which may be competitive to our products. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

***The Company is dependent upon the Company's key personnel to achieve the Company's business objectives.***

InMed depends on key personnel, the loss of any of which could harm its business. InMed's future performance and development will depend to a significant extent on the efforts and abilities of its executive officers, key employees, and consultants. The loss of the services of one or more of these individuals could harm InMed's business. InMed's success will depend largely on its continuing ability to attract, develop and retain skilled employees and consultants in our business. Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. The competition for qualified

personnel in our field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. In addition, because the Company does not currently maintain “key person” life insurance on any of the Company’s officers, employees, or consultants, any delay in replacing such persons, or an inability to replace them with persons of similar expertise, would have a material adverse effect on the Company’s business, financial condition, and results of operations.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could subject us to significant liability and harm our reputation.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with regulations of domestic or foreign regulatory authorities. In addition, misconduct by employees could include intentional failures to comply with certain development standards, to report financial information or data accurately, or to disclose unauthorized activities to us. Employee 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 our reputation. While prohibited, it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

***Our existing collaboration agreements and any that we may enter into in the future may not be successful.***

The Company also has relationships with scientific collaborators at academic and other institutions, some of whom conduct research at the Company’s request or assist the Company in formulating its research and development strategies. These scientific collaborators are not the Company’s employees and may have commitments to, or consulting or advisory contracts with, companies that conflict in interests with and pose a competitive threat to InMed. Moreover, to the extent that we decide to enter into collaboration agreements, we will face significant competition in seeking appropriate collaborators. Collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish, implement and maintain collaborations or other alternative arrangements if we choose to enter into such arrangements and our selected partners may be given, and may exercise, a right to terminate their agreement with us without cause. The terms of any collaboration or other arrangements that we may establish may not be favorable to us.

***Risks Relating to InMed’s patents, proprietary technology, and other intellectual property.***

Our success will depend, in part, on our ability to obtain patents, protect our trade secrets and operate without infringing on the proprietary rights of others. Patents and other proprietary rights are essential to the Company’s business. We rely on trade secret, patent, copyright and trademark laws, and confidentiality and other agreements with employees and third parties, all of which offer only limited protection. The Company’s general policy has been to file patent applications to protect its inventions and improvements to its inventions that are considered important to the development of its business. In certain cases, such as with our bioinformatics platform, we have chosen to protect our intellectual property by treating it as confidential internal know-how. The Company’s success will depend in part on its ability to obtain patents, defend patents, maintain internal know-how/trade secret protection and operate without infringing on the proprietary rights of others. Interpretation and evaluation of pharmaceutical patent claims present complex legal and factual questions. Further, patent protection may not be available for some of the products or technology we are developing. If we are placed in a position where we must spend significant time and money defending or enforcing our patents, designing around patents held by others or licensing patents or other proprietary rights held by others, our business, results of operations and financial condition may be harmed. In seeking to protect the Company’s inventions using patents it is important to note that there can be no assurance that:

- patent applications will result in the issuance of patents;
- additional proprietary products developed will be patentable;
- patents issued will provide adequate protection or any competitive advantages;

- patents issued will not be successfully challenged by third parties;
- commercial exploitation of the Company's inventions does not infringe the patents or intellectual property of others; or
- the Company will be able to obtain any extensions of the patent term.

A number of pharmaceutical, biotechnology and medical device companies and research and academic institutions have developed technologies, filed patent applications or received patents on various technologies that may be related to the business of the Company. Some of these technologies, applications or patents could limit the scope of the patents, if any, that the Company may be able to obtain. It is also possible that these technologies, applications or patents may preclude the Company from obtaining patent protection for its inventions. Further, there may be uncertainty as to whether the Company may be able to successfully defend any challenge to its patent portfolio. Moreover, the Company may have to participate in derivation proceedings, *inter partes* review proceedings, post-grant review proceedings, or opposition proceedings in the various jurisdictions around the world. An unfavorable outcome in a derivation proceeding, an *inter partes* review proceeding, a post-grant review proceeding, or an opposition proceeding could preclude the Company or its collaborators or licensees from making, using or selling products using the technology, or require the Company to obtain license rights from third parties. It is not known whether any prevailing party would offer a license on commercially acceptable terms, if at all. Further, any such license could require the expenditure of substantial time and resources and could harm the business of the Company. If such licenses are not available, the Company could encounter delays or prohibition of the development or introduction of the product of the Company. In the case of intellectual property where we have chosen to protect it by treating it as internal know how, such as with our bioinformatics platform, there can be no assurance that others with greater expertise or access to greater resources do not develop similar or superior technology that impairs the competitive value of our internal know-how.

***InMed's insurance may be insufficient to cover losses that may occur as a result of its operations.***

InMed currently maintains directors and officers' liability insurance and property and general liability insurance and intends in the future to obtain shipping and storage insurance for product candidates and clinical trial insurance. This insurance may not remain available to us or be obtainable by us at commercially reasonable rates, and the amount of our coverage may not be adequate to cover any liability we incur. Future increases in insurance costs, coupled with the increase in deductibles, will result in higher operating costs and increased risk. If the Corporation were to incur substantial liability and such damages were not covered by insurance or were in excess of policy limits, or if the Corporation were to incur such liability at a time when it is not able to obtain liability insurance, its business, results of operations and financial condition could be materially adversely affected.

***Our product candidates contain compounds that may be classified as "controlled substances", the use of which may generate public controversy.***

Since our product candidates contain substances related to the cannabis plant and may therefore be classified as "controlled substances", their regulatory approval may generate public controversy. Political and social pressures and adverse publicity could lead to delays in approval of, and increased expenses for our product candidates. These pressures could also limit or restrict the introduction and marketing of our product candidates. Adverse publicity from cannabis misuse or adverse side effects from cannabis or other cannabinoid products may adversely affect the commercial success or market penetration achievable for our product candidates. The nature of our business attracts a high level of public and media interest, and in the event of any resultant adverse publicity, our reputation may be harmed. Furthermore, if our product candidates are classified as "controlled substances", they may be subject to import/export and research restrictions that could delay or prevent the development of InMed's products in various geographical jurisdictions.

***There may be changes in laws, regulations and guidelines which are detrimental to our business.***

InMed's operations are subject to a variety of laws, regulations and guidelines relating to pharmacology, cannabinoids, and drug delivery, as well as laws and regulations relating to health and safety, the conduct of operations, and the protection of the environment. While, to the knowledge of the Company's management, InMed is currently in compliance with all such laws, changes to such laws, regulations and guidelines due to matters beyond the control of

the Company may cause adverse effects to our operations and financial condition. These changes may require the Company to incur substantial costs associated with legal and compliance fees and ultimately require the Company to alter its business plan. In addition, if the governments of Canada or the United States were to enact or amend laws relating to our industry, it may decrease the size of, or eliminate entirely, the market for the Company's products, may introduce significant new competition into the market and may otherwise potentially materially and adversely affect the Company's business, results of operations, and financial condition.

***Deficiencies in disclosure controls and procedures and internal controls over financial reporting could result in a material misstatement in InMed's financial statements.***

InMed could be adversely affected if there are deficiencies in its disclosure controls and procedures or in its internal controls over financial reporting. The design and effectiveness of InMed's disclosure controls and procedures and its internal controls over financial reporting may not prevent all errors, misstatements or misrepresentations. Consistent with other entities in similar stages of development, the Company has a limited number of employees currently in the accounting group, limiting the Company's ability to provide for segregation of duties and secondary review. A lack of resources in the accounting group could lead to material misstatements resulting from undetected errors occurring from one individual performing primarily all areas of accounting with limited secondary review. Deficiencies in internal controls over financial reporting which may occur could result in material misstatements of InMed's results of operations, restatements of financial statements, a decline in the price of the Common Shares or Listed Warrants, or otherwise materially adversely affect InMed's business, reputation, results of operations, financial condition or liquidity.

***Changes to International Financial Reporting Standards may adversely impact the manner in which InMed reports its financial position and operating results.***

In February 2008, the Accounting Standards Board of Canada confirmed its decision to require that all publicly accountable enterprises report under International Financial Reporting Standards, or IFRS, for interim and annual financial statements. InMed is required to report under IFRS. There are ongoing projects conducted by the International Accounting Standards Board, and joint projects with the Financial Accounting Standards Board in the U.S. that are expected to result in new pronouncements that continue to evolve, which could adversely impact the manner in which InMed reports its financial position and operating results.

***Our proprietary information, or that of our customers, suppliers and business partners, may be lost or we may suffer security breaches.***

In the ordinary course of our business, we may collect and store sensitive data, including intellectual property, data from preclinical studies, clinical trial data, our proprietary business information and that of our customers, suppliers and business partners, and personally identifiable information of our customers, clinical trial subjects and employees, in our data centers and on our networks. 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 vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Although to our knowledge we have not experienced any such material security breach to date, 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, regulatory penalties, disrupt our operations, damage to our ability to obtain patent protection for our product candidates, damage to our reputation, and cause a loss of confidence in our products and our ability to conduct clinical trials, which could adversely affect our business and reputation and lead to delays in gaining regulatory approvals.

***Failure of our information technology systems could significantly disrupt the operation of our business.***

Our business increasingly depends on the use of information technologies, which means that certain key areas such as research and development, production and sales are to a large extent dependent on our information systems or those of third party providers. Our ability to execute our business plan and to comply with regulators requirements with respect to data control and data integrity, depends, in part, on the continued and uninterrupted performance of our

information technology systems, or IT systems and the IT systems supplied by third-party service providers. These IT systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite network security and backup measures, some of our servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Despite the precautionary measures we and our third-party service providers have taken to prevent unanticipated problems that could affect our IT systems, sustained or repeated system failures or problems arising during the upgrade of any of our IT systems that interrupt our ability to generate and maintain data, and in particular to operate our technology platform, could adversely affect our ability to operate our business.

### **Risks Related to the Company's Securities**

#### ***The market prices for InMed's Common Shares and Listed Warrants are volatile and will fluctuate.***

The market price for our Common Shares and Listed Warrants may be volatile and subject to wide fluctuations in response to numerous factors, many of which are beyond InMed's control, including the following: (i) actual or anticipated fluctuations in InMed's quarterly financial results; (ii) recommendations by securities research analysts; (iii) changes in the economic performance or market valuations of other issuers that investors deem comparable to InMed; (iv) addition or departure of InMed's executive officers and other key personnel; (v) release or expiration of lock-up or other transfer restrictions on outstanding Common Shares and Listed Warrants; (vi) sales or perceived sales of additional Common Shares and Listed Warrants; (vii) liquidity of the Common Shares and Listed Warrants; (viii) significant acquisitions or business combinations, strategic partnerships, joint ventures or capital commitments by or involving InMed or its competitors; and (ix) news reports relating to trends, concerns, technological or competitive developments, regulatory changes and other related issues in InMed's industry or target markets. Financial markets often experience significant price and volume fluctuations that affect the market prices of equity securities of public entities and that are, in many cases, unrelated to the operating performance, underlying asset values or prospects of such entities. Accordingly, the market price of the Common Shares and Listed Warrants may decline even if InMed's operating results, underlying asset values or prospects have not changed. Additionally, these factors, as well as other related factors, may cause decreases in asset values that are deemed to be other than temporary, which may result in impairment losses. As well, certain institutional investors may base their investment decisions on consideration of InMed's environmental, governance and social practices and performance against such institutions' respective investment guidelines and criteria, and failure to meet such criteria may result in limited or no investment in the Common Shares and Listed Warrants by those institutions, which could materially adversely affect the trading price of the Common Shares and Listed Warrants. There can be no assurance that continuing fluctuations in price and volume will not occur. If such increased levels of volatility and market turmoil continue for a protracted period of time, InMed's operations could be materially adversely impacted and the trading price of the Common Shares and Listed Warrants may be materially adversely affected.

#### ***Raising additional capital may cause dilution to the Company's shareholders, restrict the Company's operations or require the Company to relinquish rights to its technologies or drug candidates.***

The continued development of the Company is expected to require additional financing. In order to meet its financing needs, the Company may issue a significant number of additional Common Shares and warrants to purchase Common Shares. The precise terms of any future financing will be determined by the Company and potential investors and such future financings may significantly dilute its shareholders' percentage ownership in the Company. Additionally, if the Company raises additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, it may have to relinquish valuable rights to its technologies, future revenue streams, research programs or drug candidate or grant licenses on terms that may not be favourable to the Company and/or that may reduce the value of its Common Shares.

#### ***Common shareholders are subordinated to InMed's lenders.***

In the event of bankruptcy, liquidation or reorganization of InMed, holders of its debt and its trade creditors will generally be entitled to payment of their claims from the assets of InMed before any assets are made available for distribution to InMed or shareholders. The Common Shares are effectively subordinated to the debt and other obligations of InMed.

***Future offerings of debt or equity securities may rank senior to Common Shares.***

If InMed decides to issue debt or equity securities in the future ranking senior to the Common Shares or otherwise incur additional indebtedness, it is possible that these securities or indebtedness will be governed by an indenture or other instrument containing covenants restricting InMed's operating flexibility and limiting InMed's ability to pay dividends to shareholders. Additionally, any convertible or exchangeable securities that InMed issues in the future may have rights, preferences and privileges, including with respect to dividends, more favorable than those of Common Shares and may result in dilution to shareholders. Because InMed's decision to issue debt or equity securities in any future offering or otherwise incur indebtedness will depend on market conditions and other factors beyond InMed's control, InMed cannot predict or estimate the amount, timing or nature of InMed's future offerings or financings, any of which could reduce the market price of the Common Shares and dilute the value of the Common Shares.

***Future sales of Common Shares by officers and directors may negatively impact the market price for the Common Shares.***

Subject to compliance with applicable securities laws, directors and officers of InMed and their affiliates may sell some or all of their Common Shares in the future. No prediction can be made as to the effect, if any, such future sales of Common Shares may have on the market price of the Common Shares prevailing from time to time. However, the future sale of a substantial number of Common Shares by the directors and officers of InMed and their affiliates, or the perception that such sales could occur, could adversely affect prevailing market prices for the Common Shares.

***Limited Market for Securities***

The Company's Common Shares and Listed Warrants are listed on the TSX, and the Common Shares are listed on the OTCQX® Best Market; however, there can be no assurance that an active and liquid market for the Common Shares and Listed Warrants will develop or be maintained and an investor may find it difficult to resell any securities of the Company.

***Listed Warrants***

InMed's Listed Warrants, issued on June 21, 2018, are listed on the TSX (symbol "IN.WT"). The liquidity of the trading market in InMed's Listed Warrants and the sale price, if any, for such Listed Warrants, may be adversely affected by, among other things:

- changes in the overall market for the Listed Warrants;
- changes in the Company's financial performance or prospects;
- changes or perceived changes in the Company's creditworthiness;
- the prospects for companies in the industry generally; and
- the number of holders of the Listed Warrants.

***Unlisted Warrants***

Only InMed's Listed Warrants, issued on June 21, 2018, are listed on the TSX (symbol "IN.WT"). The remainder of InMed's outstanding share purchase warrants are not listed on any exchange (the "Unlisted Warrants"), and the Company does not intend to list these Unlisted Warrants on any exchange. Investors may be unable to sell InMed's Unlisted Warrants at the prices desired or at all. There is no existing trading market for InMed's Unlisted Warrants and there can be no assurance that a liquid market will develop or be maintained for such Unlisted Warrants, or that an investor will be able to sell any of such Unlisted Warrants at a particular time (if at all). The liquidity of the trading market in InMed's Unlisted Warrants and the sale price, if any, for such Unlisted Warrants, may be adversely affected by, among other things:

- changes in the overall market for the Unlisted Warrants;

- changes in the Company's financial performance or prospects;
- changes or perceived changes in the Company's creditworthiness;
- the prospects for companies in the industry generally;
- the number of holders of the Unlisted Warrants; and
- the interest of securities dealers in making a market for the Unlisted Warrants.

***The Company does not currently pay dividends on its Common Shares and has no intention to pay dividends on its Common Shares for the foreseeable future.***

No dividends on the Common Shares have been paid by the Company to date. The Company does not intend to declare or pay any cash dividends in the foreseeable future. Payment of any future dividends will be at the discretion of the Company's board of directors, after taking into account a multitude of factors appropriate in the circumstances, including the Company's operating results, financial condition and current and anticipated cash needs. In addition, the terms of any future debt or credit facility may preclude the Company from paying any dividends unless certain consents are obtained and certain conditions are met.

### ***Tax Risk***

Prospective investors should be aware that the purchase of any of InMed's securities may have tax consequences in Canada and other jurisdictions. Prospective investors should consult with their own independent tax advisor before purchasing any of InMed's securities.

***We are exposed to risks related to currency exchange rates.***

We currently conduct a portion of our operations outside of Canada and we expect this to increase significantly in the future. Because our financial statements are presented in Canadian dollars, changes in currency exchange rates have had and could have a significant effect on our operating results. Exchange rate fluctuations between local currencies and the Canadian dollar create risk in several ways, including the following: weakening of the Canadian dollar may increase the Canadian dollar cost of international research and development expenses and the cost of sourced product components outside Canada; strengthening of the Canadian dollar may decrease the value of our revenues denominated in other currencies; the exchange rates on non-Canadian dollar transactions and cash deposits can distort our financial results; and commercial product pricing and profit margins are affected by currency fluctuations.

**For all of the aforesaid reasons and others set forth in this AIF, an investment in the Common Shares and any other securities that may be offered by InMed from time to time involve a certain degree of risk. Any person considering an investment in the Common Shares or any other securities of the Company should be aware of these and other factors set forth in this AIF and should consult with his or her legal, tax and financial advisors prior to making an investment in the Common Shares or any other securities of the Company that may be offered from time to time. The Common Shares and any other securities of the Company that may be offered from time to time should only be purchased by persons who can afford to lose all of their investment.**

## **GENERAL DEVELOPMENT OF THE BUSINESS**

InMed is a preclinical stage biopharmaceutical company specializing in the research and development of novel, cannabinoid-based therapies combined with innovative drug delivery systems. InMed conducts research, discovery, preclinical, clinical, regulatory, manufacturing and commercial development activities for its product candidates. The three core asset groups of the Company, namely, the bioinformatics platform, the biosynthesis manufacturing process, and the drug development programs, are discussed in detail below.

### **Three Year History**

On October 28, 2015, the Company entered into a purchase agreement, or the Patent Purchase Agreement, with Dr. Sazzad Hossain, the Company's Chief Scientific Officer, to acquire certain intellectual properties from Dr. Hossain,

in return for the obligation of the Company to issue 1,000,000 Common Shares to Dr. Hossain. The 1,000,000 Common Shares have an aggregate recorded value of \$140,000, or \$0.14 per share, as determined by the closing price of the Common Shares on the Canadian Securities Exchange (where InMed's Common Shares were then listed) on October 28, 2015.

Effective March 26, 2018, the Company commenced trading on the TSX under the symbol "IN". In conjunction with its listing on the TSX, the Company's shares ceased trading on the CSE. Effective May 4, 2018, the Company's common shares commenced trading on the OTCQX® Best Market under the symbol "IMLFF". In conjunction with this listing, the Company's common shares ceased trading on the OTCQB® Venture Market.

The operations of the Company for the past three fiscal years, including its drug development, delivery technologies and biosynthesis programs, are summarized below.

### **Development of a Therapy for Epidermolysis Bullosa**

InMed's lead compound is INM-750, a proprietary, topical cannabinoid product candidate intended as a therapy in epidermolysis bullosa, or EB, patients for symptom relief and, potentially, as a therapy to reverse the underlying disease in certain patient subtypes. EB is a genetic disorder that affects individuals from birth and is characterized by fragile skin that is easily damaged, leading to extensive blistering and wounding. InMed utilized its bioinformatics platform to identify cannabinoid candidates that may serve as a treatment for EB. To validate the finding of the bioinformatics platform, the Company entered into a collaborative research contract with Dr. Tamás Bíró MD, PhD, DSc of the University of Debrecen, Hungary for a one-year term commencing on February 28, 2015. Dr. Bíró has extensive research experience in studying the endocannabinoid system and the closely related transient receptor potential channels in various human diseases. The collaborative research agreement with Dr. Bíró provides that InMed owns, and shall retain, all rights, title and interest in any and all intellectual property developed from the research conducted under the agreement. The work under this agreement has been completed.

Key milestones for the EB program include:

- August 6, 2015 – the Company reported positive response from its preclinical research on INM-750 tested in various *in vitro* assays. By modulating the expression of various keratin genes that are responsible for cytoskeleton intermediate filaments and/or wound healing using INM-750, we sought to alleviate the EBS symptoms. These preliminary results validated InMed's approach as INM-750 displayed modulation of expression of various keratin genes.
- November 4, 2015 – InMed released additional preliminary preclinical data for INM-750 demonstrating positive effects in both wound healing/skin regeneration and in reducing inflammation, two key hallmarks of EB.
- May 18, 2016 – InMed reported additional preclinical results showing INM-750 demonstrated positive pain relieving effects in animal models. INM-750 animal data showed a reduction in both acute and chronic pain.
- May 4, 2017 – the Company filed an application with the Canadian Intellectual Property Office as a Patent Cooperation Treaty, or PCT, patent application, Serial No. CA2017050546 titled, "A Cannabinoid-Based Topical Therapy for Diseases and Conditions Associated with Intermediate Filament Dysfunction".
- June 13, 2017 – InMed announced it has signed an agreement with Pharmaseed Ltd, Israel's largest GLP-certified pre-clinical contract research organization, to develop a final formulation for INM-750.
- July 10, 2017 – InMed announced it has entered into a research and development collaboration with ATERA SAS of France, a leading tissue engineering company specializing in the development of advanced human tissue models. Under the terms of the agreement, ATERA will develop 3D human skin models of EB to evaluate the *in vitro* drug efficacy of INM-750. ATERA will also investigate the beneficial effects of topically applied INM-750 at ultra-structural cellular and molecular levels on *in vitro* 3D reconstructed human full thickness (dermis-epidermis) skin models composed of both normal and EB-derived skin cells. On April 6, 2018, under the terms of the Agreement, InMed and ATERA agreed to transfer the execution of the collaborative research to the Fraunhofer Institute in Germany.

- During fiscal 2018, the Company worked with Pharmaseed Ltd, Israel's largest GLP-certified pre-clinical contract research organization, and other contractors to (i) develop a final formulation for INM-750; and (ii) initiate work on IND-enabling pharmacology and toxicology studies that are required before INM-750 could be used in clinical studies.

It is anticipated that InMed will be discussing its clinical development plans with regulatory bodies in the first half of calendar year 2019. After further data analysis in preparation for our discussions with regulatory authorities, InMed has determined that additional pre-clinical pharmacology experiments are warranted. In particular, these experiments will help the Company better understand the contributions of each cannabinoid component as well as their final combination in INM-750. Specifically, these additional pre-clinical experiments will focus on the effects these compounds have on wound healing and the reduction of inflammation. InMed now expects to file its Investigational New Drug ("IND") application for INM-750 in the second half of calendar year 2019. These additional pre-clinical pharmacology experiments will be designed to ensure that INM-750 meets the clinical needs of EB patients and improve the overall prospects of success for the INM-750 development program.

### **Development of a Therapy for the Treatment of Glaucoma**

Glaucoma is characterized by an increase in intraocular pressure ("IOP"), leading to neural damage and blindness. Increased IOP is caused by increased aqueous humor, or AH, outflow resistance and/or over-production of AH. Therefore, lowering IOP is the primary physiological target for current glaucoma therapies. In order to discover which cannabinoid compounds would be active in glaucoma, InMed utilized the bioinformatics platform to compile a list of genes that are associated with pathogenesis of glaucoma disease. INM-085 is InMed's topical (eye drop) formulation containing a combination of cannabinoids as the active ingredients for the treatment of glaucoma. InMed previously reported that INM-085 is able to increase vascular diameter in the retina of mice, which is associated with reduced IOP. This approach also afforded neuroprotection to the ocular nerve in this experiment.

### **Development of an Ocular Delivery System**

To address the high rate of non-compliance with current glaucoma therapies, as well as to address the highly lipophilic nature of cannabinoids, InMed has developed an innovative drug delivery system. In 2014, the Company formed an exclusive strategic collaboration with Dr. Vikramaditya Yadav of the Department of Chemical and Biological Engineering at the University of British Columbia, or UBC, to develop a targeted drug delivery system for ocular disease. The development process focuses on a nanoparticle-based hydrogel delivery system for INM-085 and future ocular therapies. The delivery system is currently under investigation in *in vitro* and *in vivo* animal models.

Additional milestones for the ocular program include:

- May 10, 2017 – InMed announced the filing of a patent (US62/503,258) entitled, "Ocular Drug Delivery Formulation" for INM-085 as a cannabinoid-based topical (hydrogel) therapy for glaucoma. InMed is developing a stimulus-responsive, nanoparticle-laden vehicle for controlled delivery of ophthalmic drugs into the aqueous humor of the eye. The first applications of this vehicle will be for INM-085 as a cannabinoid-based topical therapy to reduce the intraocular pressure associated with glaucoma.
- October 24, 2017 - InMed announced results from a study co-sponsored by InMed (Dr. Sazzad Hossain, Chief Scientific Officer) and University of British Columbia (laboratories of Profs. Vikramaditya Yadav and Ujendra Kumar). To InMed's knowledge, the InMed-UBC study is the first ever to report hydrogel-mediated cannabinoid nanoparticle delivery into the eye, resulting in enhanced drug uptake via the cornea and lens. This study further evidences the Company's capacity to conduct a wide spectrum of drug development activities, including:
  - biosynthesis of a cannabinoid using a proprietary *E. coli*-based system;
  - packaging the cannabinoid as a nanoparticle;
  - formulation of a cannabinoid drug candidate into a novel, tissue specific delivery vehicle; and
  - confirmation of drug delivery and diffusion into a target tissue.
- March 6, 2018 – InMed announced the publication of data on its glaucoma / hydrogel formulation program in the peer-reviewed journal [Drug Delivery and Translational Research](#). The article, titled "A stimulus-responsive, in situ forming, nanoparticle-laden hydrogel for ocular drug delivery", presents results from pre-

clinical studies co-sponsored by InMed and was co-authored by Dr. Sazzad Hossain, InMed's Chief Scientific Officer and conducted at the labs of Drs. Vikramaditya Yadav and Ujendra Kumar at the University of British Columbia. In these studies, the investigators successfully validated the efficient transport of the formulated product in whole-eye experiments. The work seamlessly combined product design, synthetic biology, polymer rheology, and analysis of mass transport within ocular tissue. The hydrogel was formulated as a composite of hyaluronic acid (HA) and methylcellulose (MC). Both polymers are biocompatible and highly muco-adhesive, making them ideal candidates for an ocular formulation. The amphiphilic nanoparticles were composed of a block copolymer composed of poly-ethylene oxide (PEO) and poly-lactic acid (PLA), designed to facilitate enhanced cannabinoid drug delivery into the eye via the cornea. For this study, the non-psychoactive cannabinoid cannabigerolic acid (CBGA) was biosynthesized using InMed's proprietary *E. coli*-based manufacturing approach. Results from the experiment verified the performance of a stimulus-responsive switching between thixotropy (thinning of the gel upon a shearing force, such as blinking) and temperature-dependent rheopexy (reforming as a gel after blinking), resulting in a thin, uniform gel-like lens that holds the drug in place to allow for transcorneal transport. Envisioned as a once-per-day (at bedtime) administration, this formulation is designed to address many of the issues associated with current glaucoma medications.

- May 14, 2018 – InMed announced the filing of a PCT patent application for INM-085, a cannabinoid-based topical therapy for glaucoma, which includes protection of its technology in about 150 different countries, including the USA, and claims a priority date from May 8, 2017 (PCT/CA2018/050548). The PCT filing is a conversion from the provisional patent filed in May 2017.

This novel, proprietary delivery system for ocular drugs may also play an important commercial role in re-invigorating the commercial potential off-patent products that would benefit from a once-a-day dosing regimen. InMed plans to initiate discussion with potential partners to this end.

### **Development of a Therapy for the Treatment of Pain**

In 2014, the Company announced an additional therapy which was a proprietary mixture of cannabinoids and non-cannabis based active ingredients designed for the relief of joint pain associated with arthritis and joint disease. This program has since led to the following announcements:

- August 20, 2015 – InMed announced the successful completion and validation of preclinical pain modelling, noting that InMed had successfully screened different cannabinoid compounds in *in vivo* electrophysiology and *in vivo* behavioural models of nerve growth factor, or NGF, induced pain.
- July 27, 2017 – InMed announced the publication of Company-sponsored research in the European Journal of Pain. The article is titled “Delta-9-tetrahydrocannabinol decreases masticatory muscle sensitization in female rats through peripheral cannabinoid receptor activation”. The study results suggest that peripheral application of cannabinoids targeting the natural endocannabinoid receptor system (in this case, receptor CB1) may provide a valuable approach in treating severe pain. The model utilized in this study mimics muscle pain reported by sufferers of temporomandibular disorders, or TMD, that affect the jaw muscles and joint.
- October 3, 2017 – InMed announced the filing of a provisional patent application entitled “Methods and Composition for Treatment of Pain with Cannabinoids”, in the United States (#62/562,166) for INM-405 and other unique compositions as cannabinoid-based topical therapies for the treatment of pain.
- October 17, 2017 – InMed announced additional pre-clinical results in the development of INM-405 for the treatment of pain. In recent pre-clinical testing, InMed employed several methods to verify the effects of individual, non-THC (tetrahydrocannabinol, the primary psychoactive ingredient in cannabis) cannabinoids, as well as a matrix of cannabinoid combinations, delivered to treat peripheral pain:
  1. *in vivo* animal models of pain to measure the pain tolerance;
  2. *in vivo* electrophysiology recordings to measure the blockage of pain signal transmission in the peripheral nerve fibers; and
  3. *in vivo* behavioral studies to verify the central nervous system, or CNS, related side effects.

Results from these studies suggest that peripheral application of certain cannabinoid compounds, alone or in combination, is effective in the treatment of craniofacial muscle pain disorders, without any observed CNS side effects, and may be a more desirable strategy than systemic pain-relief administration.

### **Development of a Biosynthesis Process for the Manufacturing of Cannabinoids**

Manufacturing of pharmaceutical grade cannabinoids remains a challenge, especially those that are found in only trace amounts in the cannabis plant but nevertheless that may hold very important physiological benefits in humans. InMed recognized that having a reliable source of pure, pharmaceutical-grade starting materials that are bio-identical to the compounds found in nature for its products would be a critical success factor for its drug development strategy. On May 21, 2015, the Company commenced the development of a biosynthesis process for the manufacturing of cannabinoids through a research collaboration with Dr. Vikramaditya Yadav from the Department of Biological and Chemical Engineering at UBC. Utilizing the basis of a vector created by InMed, Dr. Yadav commenced a Research and Development Project titled “The Metabolic Engineering of yeast and bacteria for synthesis of cannabinoids and cannabis derived terpenoids” under a collaborative research agreement. Pursuant to the terms of this collaborative research agreement, InMed and UBC jointly own any resulting intellectual property jointly developed by InMed and UBC, InMed has sole ownership of any intellectual property created solely by InMed, and UBC has sole ownership of any intellectual property created solely by UBC. On May 31, 2017, InMed and UBC signed a Technology Assignment Agreement whereby InMed retains sole worldwide rights to all patents emergent from the technology under development in exchange for a royalty on products utilizing cannabinoids manufactured using the technology and on sub-licensing revenues. On May 15, 2018, InMed and the University of British Columbia extended their Collaborative Research Agreement for an additional three years.

InMed is developing this biosynthesis process for potential manufacturing of all 90+ naturally-occurring cannabinoids. We believe this process is unique in that the end product is bio-identical to plant-sourced cannabinoids, but benefits from the convenience, control and quality of a laboratory-based manufacturing process without the risk and high-resource requirements of agriculture growing operations. The Company believes that the approach InMed is developing is a robust and will result in high-yields of cannabinoids.

The Company, in conjunction with its collaborators at UBC, continues to advance the production platform for the bio-fermentation of cannabinoids. Optimization of the vector will continue in parallel with the identification of optimal fermentation conditions and downstream purification processes with yet-to-be announced 3<sup>rd</sup> party suppliers, who are currently being vetted. Additional milestones in this project include:

- February 16, 2016 – InMed announced a comprehensive *de novo* biosynthesis system for cannabinoids using multiple metabolic pathways engineered into a single manufacturing system to produce our target cannabinoids.
- September 12, 2017 – InMed announced the filing of a provisional patent application (#62/554,494) entitled “Metabolic Engineering of *E. Coli* for the Biosynthesis of Cannabinoid Products”.
- September 19, 2017 – InMed announced retaining the consulting services of Ben Paterson, P.E., to assist in defining the pathway for the scale-up, purification, and manufacturing strategies for InMed’s cannabinoid biosynthesis program.
- September 25, 2017 – InMed announced an update on the significant advancements in its proprietary technology for the microbial biosynthesis of cannabinoids, including, what the Company believes to be, two significant ‘firsts’:
  - new metabolic pathway for manufacturing the terpenoid family of cannabinoid precursors that is much more robust than other microbial expression systems tested by InMed;
  - first ever production of any fully-assembled ‘downstream’ cannabinoids in *E. coli*, beginning with genetic material to produce all precursors, enzymes, and synthases.
- September 11, 2018 – InMed announced that the University of British Columbia, laboratories of Prof. V. Yadav, was awarded a grant totalling \$136,000 over a three year period to off-set InMed’s committed investment for the collaborative research and development project entitled “Microbial metabolic engineering for cannabinoid biosynthesis”; and

- September 10, 2018 – InMed announced the filing of a PCT patent application for biosynthesis which claims a priority date from September 5, 2017 (PCT/CA2018/051074). The PCT filing is a conversion from the provisional patent filed in September 2017.

### **Other Preclinical R&D Programs**

InMed has conducted a broad range of R&D activities to explore other uses of cannabinoids in treating human diseases with unmet medical needs. These programs are at various early stages of development and, as non-core assets, their continued development is subject to available resources and/or our ability to find funding partners. Continued investment in each program is under review and we will make determinations as to which programs to continue based on several strategic factors. In addition, we may choose to partner some or all of these programs with external parties.

#### ***Chronic Obstructive Pulmonary Disease, or COPD***

On June 3, 2015, the Company announced that it had initiated a program to identify and evaluate cannabinoid compounds for the treatment of COPD using its bioinformatics platform. Initial drug discovery and preclinical development was completed under a service contract with members of the Department of Anesthesiology, Pharmacology & Therapeutics at UBC. Pursuant to the terms of the April 28, 2015 service contract with UBC that covers this project, all new intellectual property derived from this program is the sole property of InMed.

On December 6, 2016, InMed announced progress with the COPD program with *in vitro* assays using human lung fibroblasts (HFL-1 cell line), demonstrating that certain cannabinoid compounds are capable of affecting a specific protein in the biochemical pathway relevant to healing and fibrosis in the lung.

#### ***Neurodegenerative Diseases: Huntington's Disease***

On May 21, 2015, the Company commenced discovery efforts to develop screening tools to identify active cannabinoid compounds for the treatment of neurodegenerative diseases. Cannabinoids are a potentially rich yet largely under-exploited source of neuroprotective molecules. Neurodegenerative diseases incur high caregiver costs and greatly diminish the economic output of societies. Since there are no known treatments for these diseases, discovering drugs that reverse or limit neurodegeneration is an urgent medical priority. We focused our investigations on the treatment of Huntington's Disease. Over time, neuronal cell death resulting from Huntington's Disease becomes quite aggressive and widespread in the brain, eventually leading to patient death.

We have screened seven cannabinoid compounds for their role in neuroprotection in an *in vitro* culture model of Huntington's Disease. Based on *in vitro* screening assays, we have established three different molecular targets that can be used to screen the repertoire of phytocannabinoids in an efficient manner. Published studies and our preliminary data support the hypothesis that cannabinoids via endocannabinoid receptors play a significant role in ameliorating neurotoxicity in Huntington's Disease. Pursuant to the terms of the March 2, 2015 service contract with UBC that covers this project, all new intellectual property derived from this program is the sole property of InMed.

#### ***Breast Cancer***

The pathology of breast cancer is highly complicated and heterogeneous. Treatment failure and tumor progression in many cancers, including breast cancer, is associated with the development of drug-resistant tumor cell clones caused by genetic mutations in the malignant cells after treatment.

InMed set out to determine the role of cannabinoids and the endocannabinoid receptors in modulation of signaling pathways associated with tumor progression and suppression in research conducted at UBC. Pursuant to the terms of the March 2, 2015 service contract with UBC that covers this project, all new intellectual property derived from this program is the sole property of InMed.

Key research findings from this program include:

- We established the functional association between cannabinoids and breast cancer by determining the cannabinoid receptor expression in tumor cells.
- We established that cannabinoid receptors constitute a novel therapeutic target for breast cancer *in vitro*.

## **REGULATORY OVERVIEW**

The development of innovative new drugs is a time-consuming, expensive, and risky process. Despite these challenges, the pharmaceutical industry has been remarkably successful in developing a broad range of important new medicines. It is also a heavily regulated industry. Drugs are evaluated for safety, efficacy, and manufacturing quality as a condition of market access, and promotional messages must adhere to approved product characteristics. Drug prices also are regulated in most countries with national health insurance systems. Regulation of market access and promotion derives from uncertainty about drug safety and efficacy. These product characteristics can only be determined from accumulated experience over large numbers of patients in carefully designed trials or observational studies. The 1962 Amendments to the United States Food and Drug Agency Act extended the powers of the FDA to review safety, efficacy, manufacturing quality and promotion. Subsequent studies concluded that the safety and efficacy requirements added to the intrinsically high cost of R&D, led to launch delay of new drugs and favored large over small firms.

However, more recently the biotechnology revolution has transformed the nature of drug discovery and the structure of the industry. Increasingly, new drugs originate in small firms, which often out-license their products to more experienced firms for later-stage drug development, regulatory review, and commercialization. In any given year, the biotechnology industry may comprise a couple of thousand firms, but the identities of these firms change as new start-ups are formed and established firms grow, merge, or are acquired by other established companies.

### **Government Regulation and Product Approval**

As a preclinical stage biopharmaceutical company that intends to test, register and commercialize products in the United States and other jurisdictions, we are subject to extensive regulation by various regulatory authorities. The primary regulatory agency in the United States is the Food and Drug Administration ('FDA'), in Canada it is Health Canada, and in Europe it is the European Medicines Agency ('EMA'). Along with these three, there are other federal, state, and local regulatory agencies. In the United States, the Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations set forth, among other things, requirements for the research, testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our products. Although the discussion below focuses on regulation in the United States, we anticipate seeking approval for, and marketing of, our products in other countries.

Generally, our activities outside the United States will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Approval in the United States, Canada, or Europe does not assure approval by other regulatory agencies, although often test results from one country may be used in applications for regulatory approval in another country. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way through the EMA but country specific regulation remains essential in many respects. The April 2015 publication titled "Medicinal products in the European Union. The legal framework for medicines for human use" from the European Parliamentary Research Service gives a general overview of several aspects of European Union legislation on human medicines. A major difference in Europe, when compared to Canada and the United States, is with the approval process. In Europe, there are different procedures that can be used to gain marketing authorization in the European Union. The first procedure is referred to as the centralized procedure and requires that a single application be submitted to the EMA and, if approved, allows marketing in all countries of the European Union. The centralized procedure is mandatory for certain types of medicines and optional for others. The second procedure is referred to as national authorization and has two options; the first is referred to as the mutual recognition procedure and requires that approval is gained from one member state, after which a request is made to the other member states to mutually recognize the approval, whilst the second is referred to as the decentralised procedure which requires a member state to act as the reference member state through a simultaneous application

made to other member states.

The process of obtaining regulatory marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and may not be successful. See “*Risk Factors*”.

### **U.S. Government Regulation**

The FDA is the main regulatory body that controls pharmaceuticals in the United States, and its regulatory authority is based in the United States Federal Food, Drug, and Cosmetic Act. Pharmaceutical products are also subject to other federal, state and local statutes. A failure to comply explicitly with any requirements during the product development, approval, or post approval periods, may lead to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an IRB of a hold on clinical trials, refusal to approve pending marketing applications or supplements, withdrawal of approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. As presented on the section of the FDA’s website titled “Drug Review Process: Ensuring Drugs are Safe and Effective”, the steps required before a new drug may be marketed in the United States generally include:

- completion of preclinical studies, animal studies and formulation studies in compliance with the FDA’s Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an Investigational New Drug, or IND, application to support human clinical testing in the United States;
- approval by an Institutional Review Board (‘IRB’) at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with federal regulations and with Good Clinical Practices, or GCP, regulations to establish the safety and efficacy of the investigational product candidate for each target indication;
- submission of a New Drug Application, or NDA, to the FDA;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the investigational product candidate is produced to assess compliance with Current Good Manufacturing Practices (‘cGMP’) regulations, and to assure that the facilities, methods and controls are adequate; and
- FDA review and approval of the NDA.

### **Clinical Trials**

An IND is a request for authorization from the FDA to administer an investigational product candidate to humans. This authorization is required before interstate shipping and administration of any new drug product to humans in the United States that is not the subject of an approved NDA. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease under study, under the supervision of qualified investigators following GCPs, an international standard meant to protect the rights and health of patients with the disease under study and to define the roles of clinical trial sponsors, administrators and monitors. Clinical trials are conducted under protocols that detail the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. Each protocol involving testing on patients in the United States and subsequent protocol amendments must be submitted to the FDA as part of the IND. We have not yet submitted an IND for any clinical programs.

The clinical investigation of an investigational product candidate is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or some may be combined. As set out in the July 1997 publication “ICH E8 Guideline - General Considerations for Clinical Trials”, published by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, the three phases of clinical investigation are as follows:

- Phase 1. Phase 1 includes the initial introduction of an investigation product candidate into humans. Phase 1 clinical trials may be conducted in patients with the target disease or condition, or in healthy volunteers. These studies are designed to evaluate the safety, metabolism, pharmacokinetics, or PK, and pharmacologic actions of the investigational product candidate in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational product candidate's PK and pharmacological effects may be obtained to inform the design of Phase 2 clinical trials. The total number of participants included in Phase 1 clinical trials varies, but is generally in the range of 20 to 80.
- Phase 2. Phase 2 includes the controlled clinical trials conducted to evaluate the effectiveness of the investigational product candidate for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the product candidate. Phase 2 clinical trials are typically well controlled, closely monitored, conducted in a limited subject population and usually involving no more than several hundred participants.
- Phase 3. Phase 3 clinical trials are controlled clinical trials conducted in an expanded subject population at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the investigational product candidate has been obtained, are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the product candidate, and to provide an adequate basis for drug approval. Phase 3 clinical trials usually involve several hundred to several thousand participants. In most cases, the FDA requires two adequate and well controlled Phase 3 clinical trials to demonstrate the efficacy of the drug.

The decision to terminate development of an investigational product candidate may be made by either a health authority body, such as the FDA or IRB/ethics committees, or by a company for various reasons. The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor or the clinical monitoring board. This group provides authorization for whether or not a trial may move forward at designated check points. These decisions are based on the limited access to data from the ongoing trial. The suspension or termination of development can occur during any phase of clinical trials if it is determined that the participants or patients are being exposed to an unacceptable health risk. In addition, there are requirements for the registration of ongoing clinical trials of product candidates on public registries and the disclosure of certain information pertaining to the trials as well as clinical trial results after completion.

### **New Drug Applications**

In order to obtain approval to market a drug in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the product candidate for the proposed indication. The application includes all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company sponsored clinical trials intended to test the safety and effectiveness of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational product candidate to the satisfaction of the FDA. In most cases, the NDA must be accompanied by a substantial user fee; there may be some instances in which the user fee is waived. The FDA will initially review the NDA for completeness before it accepts the NDA for filing. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. After the NDA submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review product candidates are reviewed within ten to twelve months. The FDA can extend this review by three months to consider certain late submitted information or information intended to clarify information already provided in the submission.

The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP. The FDA may refer applications for novel product candidates that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. Product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

#### **Disclosure of Clinical Trial Information**

Sponsors of clinical trials of certain FDA regulated products, including prescription drugs, are required to register and disclose certain clinical trial information (though not specifically required for Phase 1 trials) on a public website maintained by the U.S. National Institutes of Health, or NIH. Information related to the product, patient population, phase of investigation, study sites and investigator, and other aspects of the clinical trial is made public as part of the registration. Sponsors are also obligated to disclose the results of these trials after completion. Disclosure of the results of these trials can be delayed until the product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the design and progress of our development programs.

#### **Advertising and Promotion**

As set out in the FDA's website discussion on the "The Prescription Drug Marketing Act of 1987", the FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. A product cannot be commercially promoted before it is approved. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling (package insert) approved by the FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses — that is, uses not approved by the FDA and, therefore, not described in the drug's labeling — because the FDA does not regulate the practice of medicine. However, FDA regulations impose stringent restrictions on manufacturers' communications regarding off-label uses.

#### **Post-Approval Regulations**

As set out in the FDA's website discussion on "Post Marketing Requirements and Commitments", after regulatory approval of a drug is obtained, a company is required to comply with a number of post-approval requirements. For example, as a condition of approval of an NDA, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. In addition, as a holder of an approved NDA, a company would be required to report adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply

with requirements concerning advertising and promotional labeling for any of its products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval to assure and preserve the long-term stability of the drug or biological product. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural and substantive record keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon a company and any third-party manufacturers that a company may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

### **Controlled Substances**

As described in Brian T. Yeh's 2012 publication "The Controlled Substances Act: Regulatory Requirements", the United States federal Controlled Substances Act of 1970, or the CSA, and its implementing regulations establish a "closed system" of regulations for controlled substances. The CSA imposes registration, security, recordkeeping and reporting, storage, manufacturing, distribution, importation and other requirements under the oversight of the United States Drug Enforcement Agency, or the DEA. The DEA is the federal agency responsible for regulating controlled substances, and requires those individuals or entities that manufacture, import, export, distribute, research, or dispense controlled substances to comply with the regulatory requirements in order to prevent the diversion of controlled substances to illicit channels of commerce.

Facilities that research, manufacture, distribute, import or export any controlled substance must register annually with the DEA. The DEA registration is specific to the particular location, activity(ies) and controlled substance schedule(s). For example, separate registrations are required for importation and manufacturing activities, and each registration authorizes which schedules of controlled substances the registrant may handle. However, certain coincident activities are permitted without obtaining a separate DEA registration, such as distribution of controlled substances by the manufacturer that produces them.

The DEA categorizes controlled substances into one of five schedules — Schedule I, II, III, IV, or V— with varying qualifications for listing in each schedule. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in treatment in the United States and lack accepted safety for use under medical supervision. They may be used only in federally approved research programs and may not be marketed or sold for dispensing to patients in the United States. Pharmaceutical products having a currently accepted medical use that are otherwise approved for marketing may be listed as Schedule II, III, IV or V substances, with Schedule II substances presenting the highest potential for abuse and physical or psychological dependence, and Schedule V substances presenting the lowest relative potential for abuse and dependence. The regulatory requirements are more restrictive for Schedule II substances than Schedule III substances. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist in most situations, and cannot be refilled. InMed's products are highly purified (>95%) cannabinoid compounds. In December 2016, the DEA issued a new classification code to cover marijuana extracts, and with this ruling all highly pure cannabinoids extracted from the plant are Schedule I drugs.

The DEA inspects all manufacturing facilities to review security, record keeping, reporting and handling prior to issuing a controlled substance registration. The specific security requirements vary by the type of business activity and the schedule and quantity of controlled substances handled. The most stringent requirements apply to manufacturers of Schedule I and Schedule II substances. Required security measures commonly include background checks on employees and physical control of controlled substances through storage in approved vaults, safes and cages, and through use of alarm systems and surveillance cameras. Manufacturing facilities must maintain records documenting the manufacture, receipt and distribution of all controlled substances. Manufacturers must submit periodic reports to the DEA of the distribution of Schedule I and II controlled substances, Schedule III narcotic substances, and other designated substances. In addition to an importer or exporter registration, importers and exporters must obtain a permit for every import or export of a Schedule I and II substance or Schedule III, IV and V narcotic, and submit import or export declarations for Schedule III, IV and V non-narcotics.

For drugs manufactured in the United States, the DEA establishes annually an aggregate quota for the amount of substances within Schedules I and II that may be manufactured or produced in the United States based on the DEA's estimate of the quantity needed to meet legitimate medical, scientific, research and industrial needs. The quotas apply equally to the manufacturing of the API and production of dosage forms.

The states also maintain separate controlled substance laws and regulations, including licensing, recordkeeping, security, distribution, and dispensing requirements. State Authorities, including Boards of Pharmacy, regulate use of controlled substances in each state. Failure to maintain compliance with applicable requirements, particularly as manifested in the loss or diversion of controlled substances, can result in enforcement action that could have a material adverse effect on our business, operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal prosecution.

Potential sources of API for INM-750, INM-085 and INM-405 are in the United States, Canada, Israel, Germany, Switzerland, United Kingdom, and other European countries. We may choose to conduct clinical trials for any of our drug candidates outside the United States subject to regulatory approval. We may decide to develop, manufacture or commercialize our product candidates in additional countries. As a result, we will also be subject to controlled substance laws and regulations from the various other regulatory agencies in other countries where we develop, manufacture or commercialize INM-750, INM-085 and INM-405 in the future.

### **Marketing Exclusivity**

As discussed in the May 19, 2015 issue of the "FDA/CDER SBIA Chronicles" published by the FDA, upon NDA approval of a new chemical entity, which for this purpose is defined as a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot approve any abbreviated new drug application, or ANDA, seeking approval of a generic version of that drug. Certain changes to the scope of an approval for a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA for a generic drug that includes the change. A Section 505(b)(2) NDA may be eligible for three-year marketing exclusivity, assuming the NDA includes reports of new clinical studies (other than bioequivalence studies) essential to the approval of the NDA.

An ANDA may be submitted one year before marketing exclusivity expires if a Paragraph IV certification is filed. In this case, the 30 months stay, if applicable, runs from the end of the five-year marketing exclusivity period. If there is no listed patent in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Additionally, six months of marketing exclusivity in the United States is available under Section 505A of the FDCA if, in response to a written request from the FDA, a sponsor submits and the agency accepts requested information relating to the use of the approved drug in the pediatric population. This six-month pediatric exclusivity period is not a stand-alone exclusivity period, but rather is added to any existing patent or non-patent exclusivity period for which the drug product is eligible.

### **Patent Term Extension**

As set out in the FDA's website discussion "Small Business Assistance: Frequently Asked Questions on the Patent Term Restoration Program" the term of a patent that covers an FDA approved drug may be eligible for patent-term extension, which provides patent-term restoration as compensation for the patent term lost during the FDA regulatory review process. The United States Federal Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent-term extension of up to five years beyond the expiration of the patent. The length of the patent-term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of

a patent that covers an approved drug.

### **European and Other International Government Regulation**

In addition to regulations in the United States and Canada, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Some countries outside of the United States have a similar process that requires the submission of a clinical trial application (CTA) much like the IND prior to the commencement of human clinical trials. In Europe, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

To obtain regulatory approval to commercialize a new drug under European Union regulatory systems, we must submit a marketing authorization application, or an MAA. The MAA is similar to the NDA, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Internationally, clinical trials are generally required to be conducted in accordance with GCP, applicable regulatory requirements of each jurisdiction and the medical ethics principles that have their origin in the Declaration of Helsinki.

### **Compliance**

During all phases of development (pre- and post-marketing), failure to comply with applicable regulatory requirements may result in administrative or judicial sanctions. These sanctions could include the FDA's imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, product detention or refusal to permit the import or export of products, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect.

### **Other Special Regulatory Procedures**

#### ***Fast Track Designation***

According to the discussion on the FDA's website on "Fast Track", under the Fast Track program, the sponsor of an IND may request the FDA to designate the drug candidate as a Fast Track drug if it is intended to treat a serious condition and fulfill an unmet medical need. The FDA must determine if the drug candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. Once the FDA designates a drug as a Fast Track candidate, it is required to facilitate the development and expedite the review of that drug by providing more frequent communication with and guidance to the sponsor.

In addition to other benefits such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's review period for filing and reviewing an application does not begin until the last section of the NDA has been submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

### ***Breakthrough Therapy Designation***

According to discussion on the FDA's website on "Breakthrough Therapy", the FDA may provide the Breakthrough Therapy designation to drugs to expedite the development and review of a candidate that is planned for use to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A Breakthrough Therapy designation includes all of the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program. The FDA also has an organizational commitment to involve senior management in such guidance.

### ***Orphan-Drug Designation***

As set out in the FDA website discussion on "Designating an Orphan Product: Drugs and Biological Products", the FDA may grant orphan-drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or, if the disease or condition affects more than 200,000 individuals in the United States, if there is no reasonable expectation that the cost of developing and making the drug would be recovered from sales in the United States. As set out in the EMA's website discussion on "Orphan Designation", in the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan-drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union community. Additionally, the orphan-drug designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug.

In the United States, orphan-drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax credits for certain research and user fee waivers under certain circumstances. In addition, if a product receives the first FDA approval for the indication for which it has orphan-drug designation, the product is entitled to seven years of market exclusivity, which means the FDA may not approve any other application for the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan-drug exclusivity. Orphan-drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. In the European Union, orphan-drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug approval. This period may be reduced to six years if the orphan-drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan-drug designation must be requested before submission of an application for marketing approval. Orphan-drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

### ***Priority Review (United States) and Accelerated Assessment (European Union)***

Based on results of the Phase 3 clinical trial(s) submitted in an NDA, upon the request of an applicant, a priority review designation may be granted to a product by the FDA, which sets the target date for FDA action on the application at six months from the FDA's decision on priority review application, or eight months from the NDA filing. According to the FDA website discussion on "Priority Review", this status is given where preliminary estimates indicate that a product, if approved, has the potential to provide a safe and effective therapy where no satisfactory alternative therapy exists, or a significant improvement compared to marketed products is possible. If criteria are not met for priority review, the standard FDA review period is ten months from the FDA's decision on priority review application, or 12 months from the NDA filing. The priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

According to the EMA website discussion on "Accelerated Assessment", under the Centralised Procedure in the European Union, the maximum timeframe for the evaluation of a MAA is 210 days (excluding "clock stops," when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation might be granted by the CHMP

in exceptional cases, when a medicinal product is expected to be of a major public health interest, which takes into consideration: the seriousness of the disease (e.g., disabling or life-threatening diseases); the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days.

### ***Accelerated Approval***

As set out in the FDA website discussion on “Accelerated Approval”, under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. This approval mechanism is provided for under 21CFR314 Subpart H and 21CFR601 Subpart E. In this case, clinical trials are conducted in which a surrogate endpoint is used as the primary outcome for approval. A surrogate endpoint is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. This surrogate endpoint substitutes for a direct measurement of how a patient feels, functions, or survives and is considered reasonably likely to predict clinical benefit. Such surrogate endpoints may be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. When the Phase 4 commitment is successfully completed, the biomarker is deemed to be a surrogate endpoint. Failure to conduct required post-approval studies or confirm a clinical benefit during post-marketing studies, could lead the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

### ***Rare Pediatric Disease Priority Review Voucher***

The FDA has an incentive program to stimulate development of new drugs for rare pediatric diseases that are serious or life-threatening as described in the FDA website discussion on “Rare Pediatric Disease Priority Review Voucher Program”. The drug must be a new active ingredient that has never been approved in any prior application (including any ester or salt of the active ingredient) and the rare pediatric disease application must meet the criteria for a priority review itself.

If a sponsor (a company) gets a new drug approved for such a rare and serious or life-threatening pediatric disease, they are eligible to receive a pediatric rare disease priority review voucher. The holder of such a voucher is entitled to a priority review of a different NDA at a future date, subject to certain conditions. Priority reviews are to be completed within six months instead of the usual 10 months after the 60-day filing period and acceptance of an NDA for review. The voucher can be used by the original sponsor or transferred (including by sale) to another party. Such vouchers are considered quite valuable. The EB indication would meet the criterion for being either serious or life-threatening and it might meet the criteria for a rare pediatric disease if current prevalence data for the United States indicates that 50% or more of the patients with EB are age 18 years or younger. An NDA filed for that indication might meet the requirements for receiving a priority review voucher upon approval, depending on the quality of efficacy and safety demonstrated in well-controlled clinical studies.

These vouchers, once awarded to a sponsor, are fully transferable to third parties who, in turn, can use it for priority review of any drug application, not specifically for a rare pediatric disease. Accordingly, there is a financial incentive for companies to pursue rare pediatric diseases.

### **Other Healthcare Laws and Compliance Requirements**

In the United States, our activities are potentially subject to additional regulation by various federal, state and local authorities in addition to the FDA, including, among others, the Centers for Medicare and Medicaid Services, other divisions of Health and Human Services, or HHS, (for example, the Office of Inspector General), the Department of Justice, or the DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre marketing product approvals, private “qui tam” actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals. See “Risk Factors”.

## **BUSINESS OF INMED**

### **Overview**

The Company is engaged in researching, developing, manufacturing and commercializing cannabinoid-based biopharmaceutical products to treat diseases with high unmet medical needs. Cannabinoids are a family of over 90 individual chemical components found in the cannabis plant, each of which may have important physiological impacts on the human body. When purified to pharmaceutical grade (>95% purity) and dosed either individually or in combination, cannabinoids may have a therapeutic effect in treating a wide range of diseases, including dermatological, neurological, cognitive, digestive, inflammatory, ocular and other diseases. In addition to internal development of drug candidates, the Company will also look to sell or license new drug candidates to pharmaceutical companies for further development, commercialization and distribution.

### ***Bioinformatics Platform***

The Company specializes in identifying cannabinoid drug candidates to treat specific diseases via its first core asset, a bioinformatics platform that enables the analysis of individual cannabinoid compounds and their ability, individually or in combination, to have meaningful physiologic impact on diseases and medical conditions. This bioinformatics platform analyses the structure of cannabinoids and searches for potential sites of pharmacological effect based on the structures and efficacy of existing drugs, disease etiology, and scientifically proven genomic, proteomic and metabolomics pathways. The Company expects that the bioinformatics platform, an asset protected as internal know-how, will be utilized for the discovery process to generate further intellectual property for the Company.

### ***Biosynthesis Manufacturing Process for Cannabinoids***

A second component of InMed’s core business is the metabolic engineering/manufacturing, also referred to as biosynthesis, of cannabinoid drug compounds. Metabolic engineering is the modification of a cell's metabolic network for increased production of a specific molecule. Metabolic engineering re-creates the plant pathway in a microbial host, thereby allowing industrial-scale exploitation of the pathway for production of natural products. Many pitfalls associated with the traditional plant growing, harvesting, processing, extraction and purification techniques can be avoided using biosynthesis. Unlike plant extraction, metabolic engineering allows manipulation of the natural pathway to optimize the final composition of the products. Not only is biosynthesis a higher-yielding and more resource-efficient manufacturing process, but the process and resulting products may face less regulatory obstacles than agriculturally-sourced cannabinoids. InMed has been approached by another company with an alternative *in vitro* production approach, but InMed has elected to pursue its own proprietary *in vivo* approach. On September 10, 2018, InMed announced that it had filed a PCT patent application entitled “Metabolic Engineering of *E. coli* for the biosynthesis of Cannabinoid Products” which claims a priority date from September 5, 2017 (PCT/CA2018/051074). The PCT filing is a conversion from the provisional patent filed in September 2017.

### ***Drug Development Programs***

The third component of InMed's core assets is its drug development programs. Via the bioinformatics platform, the Company has identified three potential clinical candidates that are currently at various stages of preclinical development:

- INM-750, our lead product in development for EB, a severe genetic skin disorder (according to analyst reports there are over 10,000 EB patients in North America, Europe and Japan and potential global market opportunity of US\$1 billion for EB related drugs/treatments);
- INM-085, a product in development for glaucoma, the second leading cause of blindness in the developed world (according to a February 2015 article published by Toni Clarke with Reuters, there is a global market of more than US\$5 billion for glaucoma related drugs/treatments); and
- INM-405, a product in development as a topical application to treat localized pain.

InMed is developing cannabinoid-based therapies and drugs to treat a multitude of illnesses and has conducted preliminary and/or advanced preclinical research in the following areas: dermatology, ocular disease, pain, inflammation, pulmonary disease, neurodegenerative disease and oncology.

### **Strategy**

InMed has numerous options in commercializing its various technologies. Management intends to take an opportunistic approach in this rapidly emerging sector of pharmaceutical development to maximize the return to investors/shareholders.

At the core of our activities, we are a drug development company focused on commercializing important cannabinoid-based medicines to treat diseases with high unmet medical needs. We plan to develop our therapies through early human testing, at which point we will evaluate the financial returns on a 'go-it-alone' commercialization effort versus out-licensing to third parties, who would continue to advance human testing, seek regulatory approval, and subsequent product sales and marketing.

We do not currently have an organization for the sales, marketing and distribution of pharmaceutical products. We may rely on licensing and/or co-promotion agreements with strategic collaborators for the commercialization of our products in the United States and other territories. If we choose to build a commercial infrastructure to support marketing in the United States, such commercial infrastructure could be expected to include a sales force supported by sales management, internal sales support, an internal marketing group and distribution support. To develop the appropriate commercial infrastructure internally, we would have to invest financial and management resources, some of which would have to be deployed prior to any confirmation that INM-750, INM-085, and INM-405 will be approved by regulatory authorities.

For INM-750 in EB, it is feasible that we could oversee the relatively limited clinical trials (expected to require hundreds, not thousands, of patients) and build the requisite internal commercialization infrastructure to self-market the product to EB clinics, which are limited in number and provide direct access to the vast majority of EB patients. For INM-085 in glaucoma, because of the potentially large clinical trial patient enrollees (several thousand) and the extensive sales effort required to reach the many thousand prescribing physicians, it is highly likely that we will seek a partnership early in the development process. For INM-405, the clinical trial pathway depends highly on the target indication, which may lead to either comparatively limited or very extensive patient populations.

We have developed two key enabling tools to support the drug development activities: the bioinformatics platform to match drug candidates to disease targets, and the biosynthesis manufacturing program to produce what are typically expensive cannabinoid compounds at a commercially feasible cost.

### **Products and Technologies Under Development**

InMed is developing the following technologies and products:

1. Bioinformatics platform;
2. Biosynthesis manufacturing process for cannabinoids;
3. Drug development program, currently consisting of:

- a. INM-750 for EB;
- b. INM-085 for glaucoma; and
- c. INM-405 for pain;
4. Hydrogel formulation for once-a-day eye drops; and
5. Other R&D programs.

### ***1. Bioinformatics platform***

Finding novel ways to treat and cure diseases is a fundamental challenge in biomedical research. There is a lack of reliable drug target prediction methods as reflected by the low clinical target validation success rate. Therefore, new bioinformatics approaches are required to accurately predict drug targets for a disease. Novel drug targets refer to unexploited targets that can be used for developing first-in-class drugs and combination therapies. Network-based methods have been developed for identification of unknown disease-associated genes. Early approaches for disease gene prioritization incorporated knowledge about disease linkage intervals with protein interaction networks and prioritized direct interactions of known disease genes.

InMed created a bioinformatics platform, which uses computer algorithms which can reach high-probability conclusions from massive, publicly available databases together with internal know-how of cannabinoid drugs. This tool is a “network based platform” for identification of novel plant-based therapies using: (i) comprehensive algorithms to integrate data from numerous bioinformatics databases, (ii) a database on the structure of currently approved pharmaceutical products, and (iii) an extensive database on over 200,000 phytochemicals, including cannabinoids.

InMed’s sources of data to include in its bioinformatics platform include information on:

- Chemical structures of researched molecules;
- Protein-protein interactions;
- Gene regulation;
- Epigenetic modification;
- Microarray data;
- Cell signal networks; and
- Metabolomics.

InMed uses several mathematical processes to establish gene and protein-protein interaction networks to identify possible multi-target-based approaches for therapy development for specific diseases of interest. By using a comprehensive pharmaceutical and phytochemical structures database, and by creating associations between approved pharmaceuticals (whose pharmacodynamics effects are well characterized) and phytochemicals with similar structures, InMed identifies active cannabinoids to act on above mentioned genes and proteins.

Once a series of potentially active cannabinoids are identified for a specific disease target, InMed then tests and confirms their activity in typically short, inexpensive *in vitro* and *in vivo* experimentation.



Figure #1: Interactions between various databases in InMed’s Bioinformatics platform

The bioinformatics platform has been used to identify InMed’s leading clinical candidates: INM-750 for epidermolysis bullosa, INM-085 for glaucoma, and INM-405 for pain, as well as a library of other opportunities that are earlier in the development pipeline.

The strategy for its continued advancement is to:

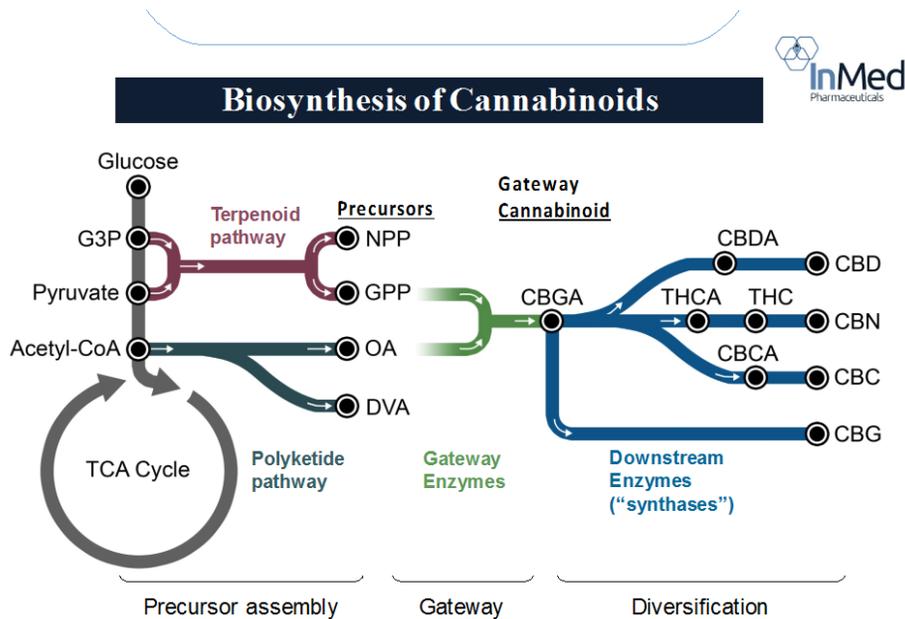
- a. Utilize databases to identify internal drug candidates for diseases / segments of strategic interest to InMed and its drug development programs; and
- b. Out-license drug candidates to third parties in those areas of low strategic interest to InMed in order to maximize revenue potential. Such licenses could potentially lead to drug supply agreements using our biosynthesis program.

## 2. *Biosynthesis manufacturing process for cannabinoids*

InMed is developing a robust, high-yielding microbial-based biosynthesis process designed for manufacturing the over 90 individual cannabinoids. InMed’s products are bio-identical to the naturally occurring cannabinoids in the cannabis plant, and the process offers superior ease, control and quality of manufacturing when compared to alternative methods.

Microorganisms do not naturally produce cannabinoids. However, utilizing genome engineering to modify their metabolism, InMed has systematically introduced the cannabis plant’s metabolic pathways into bacteria and has reported, what it believes to be, the first-of-its-kind production of downstream cannabinoids in these hosts. Briefly, InMed identified the specific gene sequences from the cannabis plant that encode the instructions to make specific cannabinoids and subsequently transplanted these genes into the bacterium *E. coli*. This intervention converts the bacterium into a manufacturing engine that produces large quantities of the target compound on demand. This development provides an opportunity for industrial-scale manufacturing of naturally occurring cannabinoids, and the Company believes it is significant improvement over existing manufacturing platforms such as direct extraction from cannabis plants or chemical synthesis. Direct extraction is quite cumbersome, time-consuming and low yielding for all but a few of the cannabinoid compounds. The use of microorganisms for manufacturing cannabinoids eliminates planting, growing, harvesting and extraction. There are also economic and environmental savings such as substantially reduced resource requirements (water, electricity, manpower, etc.). Furthermore, the agricultural approach has several hard-to-remove impurities (e.g., pesticides), potentially presenting safety issues. As with all crops, yield fluctuations present an additional risk. Only a few of the 90+ cannabinoids can be extracted from the plant in sufficient quantities to make the process economically viable. Chemical synthesis, by comparison, can be challenging and expensive due to the complexity of these molecules. For these reasons, InMed has concluded that microbial biosynthesis is superior to both of these alternative approaches.

Cannabinoids are prenylated polyketides that are derived from fatty acid and terpenoid precursors. The biosynthesis of these molecules involves four metabolic pathways, two of which originate from central carbon metabolism. The first pathway (“terpenoid pathway”, see Figure #2 below) culminates with the synthesis of geranyl pyrophosphate, or GPP, and neryl pyrophosphate, or NPP. These molecules are terpenoid building blocks, or precursors. The second cannabinoid biosynthetic pathway, the “polyketide pathway”, is a truncated version of a polyketide biosynthetic pathway and results in the second requisite precursor, either: olivetolic acid, or OA, and/or divaricic acid, or DVA. The polyketide precursors subsequently combine with the terpenoid precursors in the third pathway, which comprises a single, specialized gateway enzyme, to yield the gateway cannabinoids. For instance, OA combines with GPP to yield the gateway cannabinoid cannabigerolic acid, or CBGA. The gateway cannabinoids are subsequently modified in the fourth pathway to yield cannabinoids such as tetrahydrocannabinolic acid, or THCA, and cannabidiolic acid, or CBDA. We refer to the fourth pathway as the downstream pathway and it involves the transformation of the acid form of the cannabinoids into the non-acid form via enzymes called ‘synthases’. Synthesis of CBGA is the most dominant pathway in the plant, resulting in high quantities of the downstream cannabinoids tetrahydrocannabinol, or THC, and cannabidiol, or CBD. Other combinations of the various precursors result in different gateway cannabinoids which, in turn, leads to diversification into the 90+ cannabinoids.



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**Figure #2:** Synthesis of the gateway cannabinoid CBGA is the most prevalent pathway in the cannabis plant, leading to high levels of both THC and CBD. InMed’s technology is designed to mimic the natural biosynthesis of cannabinoids using an *E. coli* fermentation process.

InMed explored the use of several potential hosts for cannabinoid overexpression, including the bacterium *E. coli* and the yeast *S. cerevisiae*. Our preliminary investigations have identified *E. coli* as a superior host for production of cannabinoids.

We have successfully constructed the terpenoid biosynthetic pathway and the gateway pathway for synthesis of CBGA and the downstream pathways for synthesis of THCA and CBDA. Our proprietary pathway is significantly more productive than previously patented terpenoid pathways, and we have confirmed the biosynthesis of the cannabinoids using validated HPLC methodologies and 1H-NMR instrumentation.

We have constructed a series of *E. coli* strains that express variations and/or subsets of the entire biosynthetic pathway and have tested production in lab-scale fermentation tanks. Next steps in the biosynthesis program are to:

- Continue efforts to further diversify the number of cannabinoids produced using InMed's system;
- scale-up the biosynthesis process to larger vessels, where protocols will be developed to optimize manufacturing parameters; and
- identify external vendors to assist in the commercial scale-up of the process.

Options for InMed's GLP and GMP product manufacturing include building a dedicated biosynthesis facility or transferring our process/know-how to a contract manufacturing organization with existing infrastructure to produce for us the preclinical, clinical and commercial scale supply of our product candidates.

#### Targeted Benefits of Biosynthesis:

- a) Cost savings versus existing cannabis grow-harvest-extract-purify methods;
- b) Enhanced production, purification, quality control versus agricultural approaches, including avoidance of impurities (e.g. pesticides) in the final product;
- c) Increased structural integrity versus other chemical (synthetic) manufacturing methods; bio-identical to the plant compounds and no risk of random / inactive isomer production; and
- d) Access to minor cannabinoids that are currently economically unfeasible to extract from plant sources or synthesize chemically.

#### Other Applications of InMed's Biosynthesis Technology:

Currently, biosynthesis processes are used in multiple industrial applications, including use of bacteria or yeast-based systems for the production of pharmaceuticals. Other common pharmaceutical products manufactured in an *E. coli* biosynthesis process include human insulin, vitamins and antibiotics.

While the main objective in developing our biosynthesis platform technology remains to innovate a novel, efficient and cost-effective method for the production of cannabinoids for their use in InMed's R&D pipeline, we remain optimistic that there may exist additional business opportunities for us to monetize this technology. Success in this strategy will be largely dependent on the ability of biosynthesis to be price competitive.

Specifically, we are targeting three distinct potential revenue opportunities from our biosynthesis program:

- **To become a supplier of drug product to the pharmaceutical industry.**

Currently, the global annual sales estimates of GW Pharmaceutical's recently approved Epidolex® are expected to peak at ~\$2.2 billion (according to Evaluate Pharma). Beyond Epidolex®, we believe there will be additional approvals by the regulators of cannabinoid based therapies, which may create incremental business opportunities.

- **To provide raw material to the flavors and fragrance market (terpenes, etc.).**

According to the 2015 publication "Terpenoids and Their Biosynthesis in Cyanobacteria" by Pattanaik *et al*, the flavors and fragrance industries make extensive use of terpenoids and terpenes such as limonene, pinene, myrcene, caryophyllene, and linalool, all of which can be manufactured using a biosynthesis process. According to the BCC Research report entitled, "Global Markets for Flavors and Fragrances", the global market for flavors and fragrances was valued at \$26 billion in 2015. This market is expected to increase to \$37 billion by 2021. The global aroma chemicals market is currently a \$4.1 billion industry and is expected to grow to \$6.5 billion by 2021 (CAGR=12%).

- **To provide pharmaceutical-grade ingredients to the legal cannabis market.**

In addition to providing a source of raw materials (API) for InMed's therapeutic products, the biosynthesis program may play a significant role as a source of raw materials for several industries outside of the pharmaceutical segment. The role of the two most prominent cannabinoids in the cannabis plant, THC and CBD, continues to expand at an exceptional rate in the recreational, nutraceutical and 'medical marijuana' spaces, where biosynthesis may prove to

be an economical alternative to plant-sourced products. According to an October 2016 report issued by the Hemp Business Journal, the total consumer market for CBD alone is expected to surpass \$2.1 billion by 2020, up from only \$90 million in 2015. Estimates for the medical use of marijuana (delivering THC and CBD from the plant via smoking) were estimated to be \$12 billion in 2016 by Visiongain Ltd. and is estimated to surpass \$55 billion by 2025, according to Grandview Research, Inc. The worldwide sales of legal recreational cannabis are \$16.6 billion, which is expected to grow to \$35.8 billion by 2021 (CAGR=21%).

The goal in pursuing these potential revenue opportunities is two-fold: (1) introduce a revenue stream to the Company well before the expected commercial approval of our therapeutic programs, and (2) increase value to our shareholders by extending overall valuation opportunities for the underlying Company. Towards that end, in a September 2017 report entitled “The pharmaceuticals CDMO industry is consolidating – Opportunities for current players and new entrants”, Ernst and Young estimates that the valuations of North American based contract development and manufacturing organizations (“CDMOs”) have captured the highest premium in the context of acquisitions, with median deal multiple of enterprise value (EV) / LTM-revenues around 3x, and of EV/LTM-EBITDA approximately 15x.

#### Key milestones:

On May 21, 2015, the Company commenced the development of its biosynthesis process for the manufacturing of cannabinoids through a research collaboration with Dr. Vikramaditya Yadav from the Department of Biological and Chemical Engineering at UBC. Utilizing the basis of a vector created by InMed, Dr. Yadav commenced a Research and Development Project titled “The Metabolic Engineering of yeast and bacteria for synthesis of cannabinoids and cannabis derived terpenoids” under a collaborative research contract with InMed. Pursuant to the terms of this collaborative research agreement, InMed and UBC jointly own any resulting intellectual property jointly developed by InMed and UBC, InMed has sole ownership of any intellectual property created solely by InMed, and UBC has sole ownership of any intellectual property created solely by UBC. On May 31<sup>st</sup>, 2017, InMed and UBC signed a Technology Assignment Agreement whereby InMed retains sole worldwide rights to all patents emergent from the technology under development in exchange for a royalty on products utilizing cannabinoids manufactured using the technology and on sub-licensing revenues. On May 15, 2018, InMed and the University of British Columbia extended their Collaborative Research Agreement for an additional three years.

The Company, in conjunction with its collaborators at UBC, continues to advance the production platform for the bio-fermentation of cannabinoids. Optimization of the vector will continue in parallel with the identification of optimal fermentation conditions and downstream purification processes with yet-to-be announced 3<sup>rd</sup> party suppliers, who are currently being vetted.

#### Other key milestones include:

- February 16, 2016 – InMed announced a comprehensive *de novo* biosynthesis system for cannabinoids using multiple metabolic pathways engineered into a single manufacturing system to produce our target cannabinoids.
- September 12, 2017 – InMed announced the filing of a provisional patent application entitled, “Metabolic Engineering of *E. coli* for the Biosynthesis of Cannabinoid Products” (#62/554,494) pertaining to the Company’s proprietary biosynthesis program for the manufacture of cannabinoids that are identical to those found in nature. We expect that this patent application, once converted into an international PCT application and pursued in key jurisdictions throughout the world, will provide significant commercial protection for InMed’s *E. coli*-based expression system to manufacture any of the 90+ cannabinoid compounds that may have a medical impact on important human diseases. This is the first in a series of patent applications directed to various aspects of the Company’s biosynthesis program.
- September 19, 2017 – InMed announced retaining the consulting services of Ben Paterson, P.E., to assist in defining the pathway for the scale-up, purification, and manufacturing strategies for InMed’s cannabinoid biosynthesis program. Mr. Paterson has nearly four decades of experience in developing pharmaceutical manufacturing and purification processes. He was previously a Senior Engineering Advisor with Eli Lilly and Company, where he spent 37 years, including 24 years in their biosynthesis division. His expertise includes first defining processes in the lab, then scaling up to pilot and commercial scale. Mr. Paterson has

conducted design, construction, operation, optimization, and troubleshooting of both large and small molecule drug facilities including the *E. coli* biosynthesis of numerous products. He brings experience in the seamless integration of biochemistry, equipment, and process control to successfully define a “process” at scale.

- September 25, 2017 - InMed announced an update on the significant advancements in its proprietary technology for the microbial biosynthesis of cannabinoids. InMed has successfully demonstrated an ability to selectively produce various “gateway” cannabinoids using genetically engineered microorganisms. These molecules can be functionalized further to produce any of the 90+ “downstream” cannabinoids found naturally in the cannabis plant. The Company is actively employing this production chassis to synthesize compounds for certain pharmaceutical research programs. InMed’s biosynthesis program has resulted in what the Company believes to be two significant ‘firsts’:
  - new metabolic pathway for manufacturing the terpenoid family of cannabinoid precursors that is much more robust than other microbial expression systems tested by InMed
  - first ever production of any fully assembled ‘downstream’ cannabinoids in *E. coli*, beginning with genetic material to produce precursors, enzymes, and synthases.
- September 11, 2018 – InMed announced that the University of British Columbia, laboratories of Prof. V. Yadav, was awarded a NSERC grant totalling \$136,000 over a three year period to support its collaborative research and development project entitled “Microbial metabolic engineering for cannabinoid biosynthesis” with InMed.
- September 10, 2018 – InMed announced the filing of a PCT patent application for biosynthesis which claims a priority date from September 5, 2017 (PCT/CA2018/051074). The PCT filing is a conversion from the provisional patent filed in September 2017.

### ***3.a. INM-750 in Epidermolysis Bullosa***

#### **3.a.1 Cannabinoid-Based Product Development for Epidermolysis Bullosa – an Introduction**

According to J.D. Fine’s 2010 publication “Inherited Epidermolysis Bullosa”, EB is a collective name of a group of genetic disorders of connective tissues characterized by skin fragility leading to extensive blistering and wounding. It affects skin and mucous membranes, particularly of the gastrointestinal tract, genitourinary and respiratory systems. It is a debilitating disease affecting a small proportion of people in the United States, thus earning it an orphan-disease status. The disease has no definitive cure and all current treatments are directed towards symptoms relief. There are, however, a number of products, mainly gene therapies, in clinical trials in which a cure is being explored, according to several recent scientific publications. As set out in Nagarkatti *et al*’s 2009 publication “Cannabinoids as novel anti-inflammatory drugs” and other publications, it is well documented that phytocannabinoids (plant-derived cannabinoid compounds) have unique anti-inflammatory, analgesic and wound healing promoting properties via several mechanisms, thus making them good candidates for use in alleviating some of the symptoms associated with EB. InMed’s bioinformatics platform has indicated a dual approach that may prove beneficial to patients: first, the ability of certain cannabinoids to play a role in addressing key disease hallmarks (wound healing, infection, pain, itch, inflammation); and second, the ability of some cannabinoids to regulate the expression of various proteins (keratins) that may compensate for reduced expression of others.

After initially utilizing its bioinformatics platform to identify specific cannabinoids as a potential combination treatment for EB, InMed subsequently signed a research agreement with the University of Debrecen, Hungary for a one year term commencing on February 28, 2015. Dr. Tamás Bíró MD, PhD, DSc of the University of Debrecen, Hungary was the lead investigator under this research agreement. Dr. Bíró has extensive research experience in studying the endocannabinoid system and the closely related transient receptor potential channels in various human diseases. Under the agreement, InMed has paid in full the total of 127,000 Euros due to the University of Debrecen. The agreement provides that InMed owns all rights, title and interest in any and all intellectual property developed from this research agreement. The work under this agreement has been completed.

#### **3.a.2 The Science behind EB**

At the most basic level, the hallmark of EB is poor anchorage of the epidermis to the dermis such that the skin and mucous membranes of the affected individuals tend to shear and blister on minimal friction. This is due to the

genetically inherited defect in certain genes (multiple genes have been shown to be associated with the different subtypes of EB) that code for some specific proteins that are concerned with maintaining the integrity of skin and mucous membranes.

There are four main subtypes of the condition according to J.D. Fine’s 2010 publication “Inherited Epidermolysis Bullosa”. Each of these subtypes can display a spectrum of phenotypic severity reflecting the types and combinations of mutations in different genes, together with modifying environmental factors. The types of mutations also determine the mode of inheritance, either autosomal dominant or autosomal recessive. Table 1 below shows the pattern of inheritance and the defective genes and proteins in each, based on management’s review of relevant scientific literature including JD Fine’s 2016 publication “Epidemiology of Inherited Epidermolysis Bullosa Based on Incidence and Prevalence Estimates from the National Epidermolysis Bullosa Registry”:

Table 1: Classification of EB types

EB Type (Prevalence)	Genetic defect	Pattern of Inheritance	Defective Protein
EB Simplex (~55% of EB population)	K <sub>5</sub>	AD	keratin-5
	K <sub>14</sub>	AR, AD	keratin-14
	TGM5, DSP, PKP1, PLEC, DST, ITGA6, ITGB4, COL17A1	AR	transglutaminase 5, desmoplakin, plakophilin-1, plectin, α6β4 integrin, type XVII collagen
	JUP	AR, AD	plakoglobin
EB Junctional (~5% of EB population)	LAMA3 (9% of cases)	AR	laminin-332, type XVII collagen, α6β4 integrin
	LAMB3 (70% of cases)		
	LAMC2 (9% of cases)		
	COL17A1 (10% of cases)		
	ITGA6, ITGB4		
EB Dystrophic (~30% of EB population)	COL7A1	AR or AD	type VII collagen
EB Kindler type (rare)	FERMT1	AR	kindlin-1

AR =Autosomal recessive; AD = Autosomal dominance.

(a) EB Simplex

This is the most common form of EB and is characterized by a lack of adhesion of the skin directly above the basement membrane (the basal layer). An estimated 55% of people with EB have EBS resulting from a genetic defect of the keratins K<sub>5</sub> and/or K<sub>14</sub>. The most common form of EBS manifests itself as blistering confined to the hands and feet while in others blistering can occur all over the body. Blistering generally appears during the neonatal period but it can also manifest itself in later childhood (or even in adult life). Painful skin blisters are accentuated by friction, especially on the feet where footwear causes increased irritation. Friction injuries tend to occur more commonly in warm weather and secondary infections are common.

(b) Junctional EB

Junctional EB is characterized by a lack of adhesion of the skin through the basement membrane and affects some 5% of those with EB. The generalized type of junctional disease (about half of cases of junctional EB) is usually fatal in infancy. This is often as a result of anemia and malnutrition due to poor feeding caused by the serious blistering in the pharynx and esophagus. The milder form of the disease can cause life-long pain and disability.

(c) Dystrophic EB, or DEB

DEB is characterized by a lack of adhesion of the skin under the basement membrane. Approximately 30% of people with EB have DEB. Patients with DEB tend to develop blisters that heal with fibrosis, leading to joint contracture,

fusion of the fingers, contractures of the mouth membranes and narrowing of the esophagus. Often the dominant inherited type of DEB is the least severe type and the patient can lead an almost normal life. However, the severity of the condition does increase with age due to scarring, syndactyly and generalized skin atrophy. Those with recessive DEB have a high chance of developing a squamous cell carcinoma, often before the age of 35.

(d) Kindler Syndrome

This type of EB is rare and usually becomes apparent at birth or soon after. This condition is called mixed type because blisters appear across the skin layers. The condition usually improves with time and can disappear. It is the only type that causes patchy discoloring (mottling) of skin exposed to the sun. Kindler syndrome is recessive.

Epidermolysis bullosa acquisita is a rare type that is not inherited. The blisters result from the immune system attacking healthy tissue by mistake. It's similar to another immune system disorder called bullous pemphigoid. It tends to cause blisters on the hands, feet and mucous membranes.

### 3.a.3 Epidemiology, Morbidity and Mortality

The most reliable figures on prevalence and incidence of EB are derived from the National EB Registry, or NEBR, which collected cross-sectional and longitudinal data on about 3,300 EB patients in the United States from 1986 through 2002. The prevalence of EB was estimated to be approximately 11 per million and the incidence approximately 20 per million live births. In the United States, assuming that mild cases of EBS are reported only 10% of the time, the affected population in the United States is approximately 12,500. Other sources cite populations of up to 25,000 in the United States.

Generalized blistering caused by any subtype may be complicated by infection, sepsis, and death especially in infancy. Severe forms of EB increase the mortality risk during infancy. In patients with EB that survive childhood, the most common cause of death is metastatic squamous cell carcinoma. This skin cancer occurs most frequently in patients with recessively inherited DEB who are aged 15-35 years. In contrast, dominantly inherited EBS and dystrophic EB and milder forms of junctional EB may not affect a patient's life expectancy adversely. Onset of EB is at birth or shortly after. The exception occurs in mild cases of EBS, which may remain undetected until adulthood or remain undiagnosed. The disease appears to have equal incidences in both sexes.

### 3.a.4 Current Treatments

As a genetic disease, EB has no cure and as an orphan-disease there are no approved products specifically for this indication. As presented in Fine and Hintner's 2009 publication "Life with epidermolysis bullosa (EB). Etiology, diagnosis, multidisciplinary care and therapy", effective management of EB patients involves a collaborative approach between several specialists, including surgeons, dermatologists, ophthalmologists, dentists, psychologists, physiotherapists and geneticists. The aim is to provide support to the patient by alleviating symptoms and managing complications; in particular, the patient caregivers must assess and act daily to treat the wound/enable wound healing, address the current level of pain and itch, provide adequate antimicrobial protection, reduce inflammation (as a source of depressed wound healing abilities) and address the emotional state of the patient.

Current medications are employed in control of pain (various types analgesics including nonsteroidal anti-inflammatory drugs, or NSAIDS, tricyclic antidepressants, gabapentin and narcotics) and pruritus (antihistamines etc.) and to address complications such as local infection and septicemia (local and systemic antibiotics). Steroids and phenytoin are also used in managing dysphagia-associated pain. Tetracycline is considered to be beneficial in improving the blistering and epithelial disadhesion. The complications of these classes of medications are well known and the drugs are most likely to further complicate the patients' conditions since they will be used on long-term basis.

The newer products currently in research also have their problems. For example, the use of bone marrow was being researched by the University of Minnesota with some promising results. However, the severe immunosuppression that bone marrow transplantation requires causes a significant risk of serious infections in patients with large scale blisters and skin erosions.

### Competitive Conditions

We are studying INM-750, our proprietary, topical cannabinoid product candidate, as first line therapy in EB patients for symptom relief and in EBS as a therapy to potentially reverse the underlying disease via upregulation of keratins.

There are no therapies approved specifically for the treatment of EB. This lack of treatment options creates a significant unmet medical need in this devastating condition. For those products currently envisioned or in clinical trials as topical treatments, wound healing and symptom relief are the primary endpoints. In terms of disease reversal in EBS, INM-750 is the only current topical treatment that we are aware of that is envisioned to have a potential effect.

There are currently three other topical formulations that are being considered for the treatment of EB: Amryt Pharma's Oleogel-S10, Castle Creek Pharmaceutical's Diacerein 1%, and Krystal Biotech's KB103. We believe that INM-750 offers specific advantages and will prove to provide the most extensive relief of symptoms with the added potential of addressing the underlying disease.

Despite preliminary data that was promising, in September 2017 the Phase 3 study with Zorblisa™ (allantoin), another topical drug in development for EB, reported no benefit over placebo and its development has ceased.

Although still many years away, other approaches have shown promise and are under investigation for the treatment/reversal of EB:

- Skin grafts with gene-modified epidermal sheets
- Stem cell transplants
- Granulocyte colony-stimulating factor (DEB)
- Gene therapy for recessive DEB; FCX-007 (gene-modified dermal fibroblasts for recessive DEB).

### 3.a.5 Regulatory Perspectives

With the overall incidence of about 20 per million live births and prevalence of 11 per million in the United States, EB is considered an orphan disease (orphanet.org). FDA defines orphan products as “those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug”. The European Medicines Agency has its own definition of orphan disease and, under the European definition, EB is also an orphan disease.

The mission of the FDA Office of Orphan Products Development (‘OOPD’) is to advance the evaluation and development of products (drugs, biologics, devices, or medical foods) that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. This arm of the agency evaluates scientific and clinical data to identify and designate products as promising for rare disease and to further advance scientific development of such promising medical products. The office also works on rare disease issues with the medical and research communities, professional organizations, academia, governmental agencies, industry, and rare disease patient groups. OOPD provides incentives for sponsors to develop products for rare diseases. The Orphan-Drug Designation program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug. The Orphan Products Grants Program (‘OPGP’) provides funding for clinical research that tests the safety and efficacy of drugs, biologics, medical devices and medical foods in rare diseases or conditions.

It is worth noting that there is a common pathway for application of orphan status for a product to both FDA and EMA, and applicants to the FDA are advised to use the common application platform. With regards to the data to be used in the application, it is expected for applicants to demonstrate that there is “promise” that the drug will be effective in treating said disease. “Promise” is interpreted to include either data from clinical trials, data from case studies/reports, data from appropriate animal models or, on rare occasions where there is no appropriate animal, data from in vitro experiments plus some supporting information.

Table 2 Regulatory Incentives for Orphan Product Development

Regulatory Authority	Incentives
FDA	7-year marketing Exclusivity
	Tax credits: Up to 50% of clinical development costs
	Prescription Drug User Fee Act fee exemption
	Scientific assistance during drug development
	Grants
	Informal involvement in joint ventures
EMA	Protocol assistance
	Reduced regulatory fees
	Access to centralized MA procedure
	10-year marketing exclusivity
	Administrative and procedural assistances for companies classified as SMEs
	Funding from the European commission (not grants)
	Further incentives for individual member states

### 3.a.6 Data Summary of Preclinical Studies for INM-750

INM-750 is a topical cannabinoid formulation that has been specifically selected to: (i) modify the underlying cause of the disease in some patients with EBS (the most common form of EB), and (ii) to treat the major symptoms of the disease in all patients with EB.

InMed has conducted several preclinical studies to confirm the findings of the bioinformatics platform to identify potential drug development pathways for a product in EB. The following data has been generated in support of these cannabinoids as a potential therapy in EB:

#### (a) Regulation of keratin production

The goal of modifying keratin production is to target the up-regulation of a potentially compensatory keratin (K<sub>15</sub>) while having no impact on the status of malfunctioning keratins (K<sub>5</sub> and K<sub>14</sub>). Under normal conditions, K<sub>5</sub> and K<sub>14</sub> combine (dimerize) to form adhesion between the epidermis and dermis. In EBS, one or both of these keratins are damaged. K<sub>15</sub> may be able to compensate by replacing K<sub>14</sub> in this equation and combining with K<sub>5</sub> to form the adhesive properties needed for normal skin structure.

Two InMed preclinical studies using both Polymerase Chain Reaction, or PCR, and Western Blot techniques show that INM-750 can up-regulate K<sub>15</sub>, thus having the potential to have positive effects on the underlying disease in EB. Additionally, INM-750 significantly increases the expression of K<sub>15</sub> in the human keratinocyte cell line (HaCaT) *in vitro* at both the proliferation stage and the differentiation stage. This sets the stage for potential disease modification (improved skin integrity) in some patients with EBS.

On July 10, 2017, InMed announced it entered into a research and development collaboration with ATERA SAS of France, a leading tissue engineering company specializing in the development of advanced human tissue models. On April 6, 2018, under the terms of the Agreement, InMed and ATERA agreed to transfer the execution of the collaborative research to the Fraunhofer Institute (“Fraunhofer”) in Germany. Under the terms of the agreement, Fraunhofer will develop 3D human skin models of EB to evaluate the *in vitro* drug efficacy of INM-750. Fraunhofer will also investigate the beneficial effects of topically applied INM-750 at ultra-structural cellular and molecular levels on *in vitro* 3D reconstructed human full thickness (dermis-epidermis) skin models composed of both normal and EB-derived skin cells. This project with Fraunhofer is designed to assess the potential of INM-750 to have an impact in disease reversal, further supporting InMed’s current data indicating an up-regulation in specific keratins in the skin.

(b) Wound-healing and skin regeneration

The major disease symptom in EB is the extensive wounds that can be generated throughout any day by simple friction on the skin, even as simple as clothes rubbing the skin. One key goal of any product to treat this disease is, therefore, an ability to facilitate accelerated wound healing via rapid skin regeneration and wound closure.

E-Cadherin is major component of epithelium integrity. During wound healing, transforming growth factor beta, or TGF- $\beta$ , causes a reduction in E-Cadherin. INM-750 was tested and its ability to rescue TGF- $\beta$ -induced down-regulation of E-Cadherin in human keratinocytes was verified in this study.

(c) Pain (and Itch) reduction

Pain is one of the key symptoms in EB and requires significant effort to monitor and treat. INM-750 has demonstrated positive pain relieving effects in NGF-induced *in vivo* pain models in rats. To further demonstrate this, we utilized *in vivo* electrophysiology where INM-750 blocks the pain signals in the neurons. From management's review of relevant scientific literature, we concluded that both pain and itch may sometimes utilize the same neural pathways and it is anticipated that a reduction in pain may also result in a reduction in itch.

(d) Reducing inflammation

Interleukin-8, or IL-8, is the most potent chemoattractant for blood neutrophils and important mediator of angiogenesis (formation of new blood vessels). Chronic IL-8 production and neutrophil activation in a skin wound is an unfavorable element of skin pathology as it leads to extensive inflammation.

Matrix metalloproteinases (MMPs) are part of the zinc-dependent endo-proteases family which modulate homeostasis of the extracellular matrix in skin. In response to skin damage and inflammation, metalloproteinases, including MMP-9, are often up-regulated. Specifically, exposure of keratinocytes, such as HaCat cells, to TNF- $\alpha$  induces expression of the inflammatory related factors such as IL-8, MCP-1, ICAM-1 and MMP9.

In our hands, INM-750 suppressed induction of IL-8 and MMP-9 in HaCat cells when exposed to both TNF- $\alpha$  and INF- $\gamma$  *in vitro*. These results suggest that INM-750 may be effective in the reduction of inflammation in the skin. Furthermore, both IL-8 and MMP-9 have been shown to be increased in the blister fluid of EBS patients, suggesting both as potential targets for EBS treatments according to a 2013 publication by Lettner *et al* entitled "MMP-9 and CXCL8/IL-8 Are Potential Therapeutic Targets in Epidermolysis Bullosa Simplex".

(e) Antimicrobial activity

InMed has not directly conducted any preclinical studies on the impact of cannabinoids as antimicrobial agents since this area has been widely studied and published. Recent third party research showed that certain cannabinoid compounds have potent antibacterial properties including against various strains of multidrug-resistant bacteria, including methicillin-resistant *S. aureus*, or MRSA. According to Appendino *et al*'s 2008 publication "Antibacterial cannabinoids from *Cannabis sativa*: a structure-activity study", results of this third party research demonstrated potent antimicrobial activity for all tested cannabinoid compounds.

(f) EBS formulation prototype development

Careful attention must be paid to any topical product to be used in EB for several reasons. Our target product is designed to be applied over major portions of the body (if not the entire body), once each day. As such, the patients, who are typically children, will be exposed to the active drug as well as the excipients of the gel, possibly for life. Great care must be given that these components will be safe over the long-term and that they will not add to the already painful condition that the patients are suffering.

Particular attention has been given to the following criteria in the formulation development for INM-750:

- The excipients are safe for extensive body surface area exposure over a long duration.

- The active ingredients (cannabinoids) are dosed at the appropriate level – high enough to provide optimal clinical effect at the treatment site but low enough to minimize any systemic exposure.
- The final formulation can be administered daily with minimal friction to the skin.

InMed utilized the Franz Cell diffusion method to assess skin penetration rates and depth for a proposed topical formulation for INM-750. The formulation is applied to skin samples and measurements are taken of how much drug penetrates to which depths in the skin. Using this method, a preliminary formulation of INM-750 achieved drug delivery to the epidermis and dermis layers as needed. Work is ongoing to optimize the delivery characteristics of the formulation. Working with well-characterized excipients, InMed is testing several slight variations in formulation to achieve the desired concentration of drug in the skin while simultaneously avoiding high drug concentrations in systemic circulation (in the blood).

During fiscal 2018, the Company worked with Pharmaseed Ltd, Israel's largest GLP-certified pre-clinical contract research organization, and other contractors to (i) develop a final formulation for INM-750; and (ii) initiate work on IND-enabling pharmacology and toxicology studies that are required before INM-750 could be used in future clinical studies

### 3.a.7 Clinical Development Plans

#### INM-750 for EB

InMed is currently in the early planning stage for its clinical development pathway for INM-750 in EB. It is anticipated that InMed will be discussing its clinical development plans with regulatory bodies in the first half of calendar year 2019. After further data analysis in preparation for our discussions with regulatory authorities, InMed has determined that additional pre-clinical pharmacology experiments are warranted. In particular, these experiments will help the Company better understand the contributions of each cannabinoid component as well as their final combination in INM-750. Specifically, these additional pre-clinical experiments will focus on the effects these compounds have on wound healing, the reduction of inflammation and itch. InMed now expects to file its Investigational New Drug (“IND”) application for INM-750 in the second half of calendar year 2019. These additional pre-clinical pharmacology experiments will be designed to ensure that INM-750 meets the clinical needs of EB patients and improve the overall prospects of success for the INM-750 development program.

We can make certain scope-estimates in terms of potential clinical trial sizes, timing and endpoints based on the recent clinical pathway followed by another phytochemical-based topical product for EB, Zorblisa™ (Amicus Therapeutics). The key finding from our review of publicly available information for the Zorblisa™ development program is that a clinical program is very focused for an orphan indication and the clinical trials do not include large numbers of patients. It would not be possible to conduct large trials for such a rare disease. Therefore, the clinical studies need to be carefully designed and controlled to allow suitable assessment of the efficacy and safety of a new therapy in a small number of patients. Broad multicenter trials are needed to recruit patients as quickly as possible. InMed will work closely with regulatory authorities and clinical experts in developing the clinical program for INM-750.

According to the Pharmaceutical Research and Manufacturers of America's “Biopharmaceutical Research & Development: The Process Behind New Medicines”, on average, it takes at least ten years for a new medicine to complete the journey from initial discovery to the marketplace, with clinical trials alone taking six to seven years on average. In certain unique cases, drugs have been approved by the FDA within 3-4 years from the commencement of clinical trials. Given that INM-750 has not yet received regulatory consent to start human clinical trials (and there can be no assurance that it will ever receive such regulatory consent), it is not possible with any degree of certainty to estimate how long it will take to complete clinical trials and potentially obtain marketing approval. To the extent that INM-750 may potentially be designated as either a Fast Track drug, a Breakthrough Therapy, or for Priority/Accelerated Review, its timeline to any potential marketing approval may be shorter than might otherwise be the case.

### 3.a.8. Commercial Opportunity for EB Products

Commercial attractiveness and valuations of therapies under development (prior to market launch) can be measured several ways. In EB, there are investment banking research reports on potential peak annual sales for the products themselves, as well as the total valuations of company and/or product acquisitions.

As first reported in Shire plc's January 8, 2013 press release, Shire plc acquired Lotus Tissue Repair, Inc., or Lotus, for total consideration of approximately US\$174 million, consisting of US\$49 million in upfront consideration and contingent consideration of US\$125 million. At the time of the transaction, Lotus had a preclinical program developing recombinant human collagen Type VII as a protein replacement therapy for Dystrophic EB, a subset of EB (approximately 30% of EB cases).

In September 2015, Amicus Therapeutics, Inc., or Amicus, completed the acquisition of Scioderm, Inc., or Scioderm, for total consideration of approximately US\$847 million, consisting of US\$229 million in upfront payments of cash and stock, US\$361 million upon the achievement of certain clinical and regulatory milestones and US\$257 million upon the achievement of certain sales milestones. Further, if a Priority Review Voucher, or PRV, would have been awarded for Zorblisa™, the lesser of \$100 million or 50% of the PRV market value would have been delivered to Scioderm shareholders. Scioderm's sole clinical asset at the time of the transaction was Zorblisa™ a Phase 3 clinical product in development for the treatment of EB. The acquisition was based on results from 42 patients in a Phase 2b clinical study of Zorblisa™.

Additionally, several sources have attempted to provide definition of the revenue opportunity for a drug that would be effective in treating EB. Estimates include:

- Cowen and Co. – In a September 2015 research report on Amicus Therapeutics, Cowen estimated the market potential for a drug that provides partial symptomatic relief in EB (Zorblisa™) as having potential maximum annual revenues of US\$1.2B.
- JP Morgan – In a similar research report from 2015 on Amicus, JP Morgan estimated peak annual sales of ~\$900M for Zorblisa™, if approved for sale.

### 3.b. INM-085 in Glaucoma

#### 3.b.1 Cannabinoid Based Medicine Development for Glaucoma – an Introduction

Glaucoma is a chronic optic neuropathy that is typically caused by high IOP. Inadequate or obstructed drainage of the aqueous humor through the trabecular mesh, which is the pathophysiology of glaucoma, increases the fluid pressure within the anterior chamber, subsequently propagating into the posterior chamber of the eye, according to Weinreb *et al's* 2014 article "The pathophysiology and treatment of glaucoma: a review". The increased intraocular pressure exacts a toll on the basal membrane of the retina, thinning the mesh-like tissue in this region and damaging the head of the optic nerve. According to Quigley and Boman's 2006 publication "The number of people with glaucoma worldwide in 2010 and 2020", glaucoma is currently the second leading cause of blindness world-wide; it is estimated to affect a population close to 80 million by 2020.

Current glaucoma remedies work by lowering intraocular pressure either by inhibiting carbonic anhydrase in the eye, or reducing the production of aqueous humor by the ciliary epithelial cells, or by increasing fluid drainage through the trabecular mesh. There is considerable room for improvement of existing drugs, most of which are formulated as eye drops, in terms of efficacy, safety, delivery, and the development of tolerance over time. According to multiple scientific articles, studies have shown that when drugs are delivered as drops, less than 5% of the dose penetrates the cornea after eye drop administration, meaning 95% of the administered drug never reaches its target. Thus, there is much room for improvement on the drug-delivery as a means of increasing clinical efficacy.

*Science behind Glaucoma*

Glaucoma is a group of eye diseases which results in damage to the optic nerve and vision loss, according to the 2016 publication “Facts about Glaucoma” from the United States National Eye Institute. The most common type is open-angle glaucoma, or OAG, with less common types including closed-angle glaucoma, or CAG, and normal-tension glaucoma. OAG develops slowly over time and there is no pain. If left untreated, side vision may begin to decrease followed by central vision resulting in blindness if not treated. CAG can present gradually or suddenly according to Mantravadi & Vadhar’s 2015 article titled “Glaucoma” in the *Primary Care* publication. The sudden presentation may involve severe eye pain, blurred vision, mid-dilated pupil, redness of the eye and nausea. Vision loss from glaucoma, once it has occurred, is permanent.

Risk factors for glaucoma include increased pressure in the eye, thinness of the cornea, a family history of the condition, age over 40 years in African Americans, and age over 60 years for everyone (especially Mexican Americans) , according to the 2016 publication “Facts about Glaucoma” from the United States National Eye Institute. High eye pressure (those with a value of greater than 21 mmHg or 2.8 kPa) is often associated with a greater risk of glaucoma. However, some people may have high eye pressure for years and never develop damage. Conversely, as reported Xue-Song Mi et al in a 2014 publication “The current research status of normal tension glaucoma”, optic nerve damage may occur with normal pressure, known as normal-tension glaucoma . The mechanism of OAG is believed to be slow exit of aqueous humor through the trabecular meshwork while in CAG the iris blocks the trabecular meshwork. Diagnosis is typically made by a dilated eye examination.

If treated early, it is possible to slow or stop the progression of disease with medication, laser treatment, or surgery. The goal of these treatments is to decrease eye pressure. A number of different classes of glaucoma medication are available. Laser treatments may be effective in both OAG and CAG. A number of types of glaucoma surgeries may be used in people who do not respond sufficiently to other measures. Treatment of CAG is a medical emergency.

### *Epidemiology*

Drawing on epidemiology information from previously cited sources, total open-angle glaucoma prevalence worldwide is estimated at 1.96% of the population, of which 75% is OAG. As of 2010, there were 44.7 million people in the world with OAG of which 2.8 million were in the United States. By 2020, the prevalence is projected to increase to 80 million worldwide and 3.4 million the United States. It occurs more commonly among older people. CAG is more common in women. Both internationally and in the United States glaucoma is the second-leading cause of blindness.

### Current Treatments in Glaucoma

Current treatments for glaucoma include medication, laser treatment and surgery. According to Mantravadi & Vadhar’s 2015 article titled “Glaucoma” in the “Primary Care” publication, the goals of glaucoma management are to avoid glaucomatous damage and nerve damage and preserve visual field and total quality of life for patients, with minimal side effects. This requires appropriate diagnostic techniques and follow-up examinations, and judicious selection of treatments for the individual patient. Although intraocular pressure is only one of the major risk factors for glaucoma, lowering it via various pharmaceuticals and/or surgical techniques is currently the mainstay of glaucoma treatment.

Current prescription eyedrop medications include:

- Prostaglandins such as latanoprost, bimatoprost and travoprost to increase the outflow of fluid from the eye and reduce ocular pressure. These can sting the eyes, darken the iris and eyelashes, and blur vision.
- Beta blockers such as timolol and betaxolol reduce ocular pressure by reducing the production of fluid in the eye. Possible side effects include wheezing or difficulty breathing, slowed heart rate, lower blood pressure, impotence and fatigue.
- Alpha-adrenergic agonists such as apraclonidine and brimonidine, both reduce the production of aqueous humor and increase the outflow of fluid from the eye. Side effects may include dry mouth, red eyes or eyelids, fatigue, low or high blood pressure, blurred vision and light sensitivity.

- Carbonic anhydrase inhibitors such as dorzolamide and brinzolamide also reduce the production of fluid in the eye, but they are associated with blurred vision, bitter metallic taste in the mouth, dry eyes, red/irritated eyes, headache, and upset stomach.

Again according to Mantravadi & Vadhar’s 2015 article titled “Glaucoma” in the *Primary Care* publication, often patients need to take multiple eye drops throughout the day. Given the side effect profiles, many patients don’t take their medications properly or at all. Surgery and laser therapies are intended to physically improve the drainage of fluid from the eyes, lowering pressure. Patients with OAG can have clogged channels in the trabecular network opened with laser therapy, filtering surgery (trabeculectomy) or electrocautery. In other cases, small drainage tubes may be implanted in the eye. Possible complications include pain, redness, infection, inflammation, bleeding, abnormally high or low eye pressure and loss of vision. Some types of eye surgery may speed the development of cataracts. Additional procedures may be needed if eye pressure continues to increase.

The table below on treatment considerations based on glaucoma severity is derived from the International Council of Ophthalmology’s 2015 “ICO Guidelines for Glaucoma Eye Care”.

Table 3: Treatment Considerations based on Glaucoma Severity

Glaucoma Severity	Findings	Suggested IOP Reduction	Treatment Considerations
Early	Optic Nerve Damage ± Visual Field Loss	Lower IOP ≥25%	<b>Medication</b> <i>or</i> Laser trabeculoplasty
Moderate/ Advanced	Optic Nerve Damage + Visual Field Loss	Lower IOP ≥25 – 50%	<b>Medication</b> <i>or</i> Laser trabeculoplasty <i>or</i> Trabeculectomy ± Mitomycin C <i>or</i> Tube (± cataract removal and intraocular lens [IOL]) <i>and/or</i> Cyclophotocoagulation ( <i>or</i> cryotherapy)
End-stage (Refractory glaucoma)	Blind Eye ± Pain	Lower IOP ≥25 – 50% (if painful)	<b>Medication</b> <i>and/or</i> Cyclophotocoagulation ( <i>or</i> cryotherapy) <i>and</i> Rehabilitation Services

### Competition for INM-085 in Glaucoma

Due to the large medical need and potentially significant commercial opportunity, the competitive landscape of glaucoma is intense. As such, there are currently over 10 medications approved by the FDA for the treatment of glaucoma, which are summarized in Table 4 below, according to drug class. In addition to the currently approved medications, there are a multitude of other therapies being evaluated in clinical trials, and many others in pre-clinical trials. Finally, it should be noted that there are several laser surgeries, and other forms of surgical procedures that are currently being performed to treat glaucoma, which also serve as a source of competition to the therapeutic alternatives.

In December 2017, the FDA approved a therapy, RHOPRESSA®, in a new class of glaucoma treatments known as Rho Kinase inhibitors, or “ROCKs”. RHOPRESSA® is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Most treatments for glaucoma are designed to lower and/or control IOP. Glaucoma eye drops often are the first choice over glaucoma surgery and can be very effective at controlling IOP to prevent eye damage. Glaucoma eye drop formulations are often prescribed in combination to achieve an additive or synergistic effect for the best IOP control.

Some people are poor candidates for various glaucoma eye drops; in particular, those who may react negatively to drug product that may reach other parts of the body. A certain percentage of the active ingredient of the medication, though small, will enter the bloodstream via vasculature in the eye and may adversely affect functions such as heart rate and breathing

INM-085 is envisioned as a once-a-day eye drop medication and will compete with treatment modalities in the ‘medicines’ category if approved for sale.

In addition to INM-085, the Company is aware of only one other pharmaceutical-grade cannabinoid-based therapy being evaluated for the treatment of glaucoma. Specifically, Nemus Biosciences (“Nemus”) is developing NB1111 (THC-Val-HS) for the treatment of glaucoma. NB1111 is a THC prodrug, which has demonstrated IOP lowering efficacy in multiple pre-clinical models, as well as increased flow trabecular mesh, increased uveoscleral outflow, decreased fluid production and, most notably, direct neuroprotection of retinal ganglion cells (RGCs), which leads to eventual blindness in patients.

The table below on medicines for glaucoma treatment is derived from information from the websites of the Glaucoma Research Foundation and the Mayo Clinic.

Table 4: Medicines for Glaucoma Treatment (IOP Lowering Drugs)

Drug Class	Leading Examples	Mode of Action / Side Effects by Class
Prostaglandins	Latanoprost (Xalatan®, Pfizer), Lumigan® (Allergan), Travatan Z® (Alcon)	Relaxes muscles in the eye's interior structure to allow better outflow of fluids. Adverse Drug Effects, or ADEs, include mild redness and stinging, change of eye color, change in the pigment of the eye lashes or eyelid skin, and lengthening and curling of the eyelashes.
Beta-blockers	Timoptic XE® (Merck), Istalol® (ISTA), Betoptic S® (Alcon)	Decrease fluid production in the eye; typically an adjunct to prostaglandins. Potential to reduce heart rate, may cause ADEs in patients with heart or lung problems, depression or other conditions.
Alpha-adrenergic agonists	Iopidine® (Alcon), Alphagan® (Allergan)	Decrease rate of aqueous humor production and increase drainage. ADEs include irregular heart rate, high blood pressure, fatigue, and red, itchy or swollen eyes.
Carbonic anhydrase inhibitors	Eyedrops: Trusopt® (Merck) and Azopt® (Alcon). Oral pills: Diamox® (Sigma), Neptazane® (Wyeth-Ayerst) and Daranide® (Merck).	Decreasing rate of aqueous humor production. ADEs include stinging, burning, eye discomfort (from eye drop form); tingling hands and feet, fatigue, stomach upset, memory problems, frequent urination (from pill form).
Miotics or Cholinergic agents	pilocarpine	Increases the outflow of aqueous humor from the eye. ADEs include smaller pupils, possible blurred or dim vision, and nearsightedness.
Rho kinase (ROCK) inhibitors	RHOPRESSA® / Netarsudil (aerie Pharmaceuticals)	Increases aqueous outflow by reversing structural and functional damage at the trabecular meshwork. Additionally, the vasodilatory effect of some ROCK inhibitors reduces episcleral venous pressure.

### Investigational Glaucoma Treatments

Despite the treatments available for lowering the IOP, there are some individuals for whom these treatments are either not tolerated due to side effects or in whom the IOP is not sufficiently lowered. In these situations, both glaucoma patient and physician look for alternative therapies.

While some experimental glaucoma medications explore new ways of controlling IOP, other treatments are directed at protecting the optic nerve (neuroprotection) to prevent eye damage, potential vision loss or even blindness. Many ongoing clinical studies are trying to find neuroprotective agents that might benefit the optic nerve and certain retinal cells in glaucoma.

Some investigational treatments are undergoing FDA clinical trials to prove safety and effectiveness. Other potential glaucoma treatments are strictly in experimental stages and may be years away from the possibility of being available on the marketplace.

### Cannabis (THC) to treat Glaucoma

Although the role of cannabinoids in treating glaucoma is thought to be very well understood, according to the 2004 publication from Tomida *et al* titled “Cannabinoids and glaucoma”, no such products are currently approved for this disease. The neuroprotective role of cannabinoids has not heretofore been utilized as a therapeutic strategy, primarily

due to great difficulties associated with the targeted delivery of cannabinoids to intraocular tissues. This class of compound is also relatively poorly bioavailable due to their low aqueous solubility.

Previously reported attempts for topical delivery of cannabinoids to the ocular tissues used formulations based on mineral oil (see Jay *et al*'s 1983 article "Multiple-drop study of topically applied 1% delta 9-tetrahydrocannabinol in human eyes") and cyclodextrins (according to multiple references). Until very recently, studies on novel topical ophthalmic formulations of cannabinoids have been largely non-existent. Nevertheless, the use of marijuana to treat glaucoma has extensive anecdotal evidence and supporting clinical data. It has been definitively demonstrated, in articles such as Merritt *et al*'s 1980 publication "Effect of marijuana on intraocular and blood pressure in glaucoma", and widely appreciated, that smoking marijuana lowers IOP in both normal individuals and in those with glaucoma. Certain drawbacks are associated with the use of (smoked) marijuana to treat glaucoma:

- Marijuana has a short duration of action (only 3-4 hours), meaning that to lower the IOP around the clock it would have to be smoked every three hours.
- Marijuana's mood altering effects, almost exclusively via the chemical tetrahydrocannabinol, or THC, would prevent the patient who is using it from driving, operating heavy machinery, and functioning at maximum mental capacity.
- Marijuana cigarettes also contain hundreds of compounds that damage the lungs, and the deleterious effect of chronic, frequent use of marijuana upon the brain is well established, as noted in K. Green's 1998 publication "Marijuana smoking vs cannabinoids for glaucoma therapy".

Other means of administering THC include oral, sublingual, and eye drop instillation. The first two avoid the deleterious effect of marijuana smoke on the lungs, but are limited by the other systemic side effects. In one study, reported on in AJ Flach's 2002 article "Delta-9-tetrahydrocannabinol (THC) in the treatment of end-stage open-angle glaucoma", in which doctors offered some of their patients with worsening glaucoma the option of pills containing tetrahydrocannabinol and/or smoking marijuana, all of them experienced side effects and 4 of 9 patients had discontinued use by either or both methods within 9 months due to side effects. Given that glaucoma is a lifelong disease, commonly requiring treatment for decades, these results strongly suggest that systemic use of THC is not a reasonable treatment option for such patients. The use of eye drops containing THC, or related compounds, has been investigated, but it has not yet been possible to formulate an eye drop that is able to introduce the drug into the eye in sufficient concentrations due to the low water solubility of the active ingredients.

Although marijuana does lower the IOP temporarily, IOP lowering is only one consideration in slowing the optic nerve damage of glaucoma. For instance, there is a growing body of evidence that inadequate blood supply to the optic nerve may contribute to glaucoma damage. Since marijuana given systemically is known to lower blood pressure, it is possible that such an effect could be deleterious to the optic nerve in glaucoma, possibly reducing or eliminating whatever beneficial effect that would be conferred by lowering IOP. For this reason, marijuana, or its components administered systemically, cannot be recommended without a long term trial which evaluates the health of the optic nerve.

An exciting finding, reported on in Jarvinen *et al*'s 2002 article "Cannabinoids in the treatment of glaucoma", is the discovery of receptors for cannabinoids in the tissues of the eye itself, suggesting that local administration has the possibility of being effective. Furthermore, there is evidence from research in the brain, as reported on in Nucci *et al*'s 2008 article "Potential roles of (endo)cannabinoids in the treatment of glaucoma: From intraocular pressure control to neuroprotection", that there may be properties of the cannabinoids that protect nerve cells like those in the optic nerve. This raises the hope that cannabinoids could protect the optic nerve not only through IOP lowering but also through a neuroprotective mechanism. However, unless a well-tolerated formulation of a marijuana-related compound with a much longer duration of action is shown in rigorous clinical testing to reduce damage to the optic nerve and preserve vision, there is no scientific basis for use of these agents in the treatment of glaucoma.

The wide variety of topically effective anti-glaucoma drugs which are available today and few others in the developmental stage represent significant advancement in ocular therapeutics. While these topical ophthalmic preparations have reduced the risk of systemic toxicity to some extent, their long term use causes systemic as well as ocular toxicity. Ophthalmologists usually select the drugs individually and replace them regularly in order to prevent the habituation phenomenon (reduction in effect of the drug over time) and negative side effects.

#### INM-085 Discovery Process:

InMed utilized its bioinformatics platform to:

- Compile a list of genes that are associated with pathogenesis of glaucoma disease from our own in-house curated disease analysis. We grouped these selected genes based on the glaucoma disease hallmarks such as trabecular meshwork, or TM, remodeling, retinal ganglion cell, or RGC, survival and genes involved in extracellular matrix, or ECM, etc.
- To better understand the relationship among selected glaucoma disease genes, we constructed a protein-protein interaction network and the graphic view of the interaction network was built for further discovery.
- We then conducted various *in vitro* and *in vivo* experiments to validate the output of the bioinformatics platform. INM-513 (InMed's internal code for a specific cannabinoid compound) proved to be a highly potent alpha-agonist targeting  $\alpha 2$ -adrenoceptor.

Glaucoma is a neurodegenerative disease in which various triggers (such as elevated IOP) induce cascades of events, which ultimately lead to apoptotic retinal ganglion cell death and result in irreversible loss of vision. However, as mentioned above, the goal of all current glaucoma therapies is to reduce IOP without including any strategies of neuroprotective treatment. In fact, some patients often fail to show much improvement even after IOP reduction, whereas others develop glaucoma in the absence of elevated IOP.

The above demonstrates our multi-drugs / multi-targets approach in action through multiple different processes. As glaucoma is a multifaceted disease, we believe that our multi-component / multi-targets approach to treat multiple processes in glaucoma disease has an advantage over the traditional one drug / one gene approach, as our approach mitigates the possibility of occurrence of drug resistance that often arises in the one drug / one gene approach.

#### Key *in vitro* results for INM-085 in Glaucoma:

InMed conducted several *in vitro* studies using surrogate biomarkers to understand the mechanism of action of INM-085. The Company expects that these results will form part of a future patent application for the treatment of glaucoma.

#### Key *in vivo* results for INM-085 in Glaucoma:

INM-085 was tested in normal mice. A total of nine mice were used in this study where the left eye was treated with vehicle (control) and right eye was treated with emulsified INM-085. After 30 minute treatment application, the retinas of the left and right eyes of each mouse were scanned with Spectral Domain Optical Coherence Tomography, which utilizes interferometry to create cross-sectional views of the retina. This non-invasive technique is used to detect and monitor morphological changes of ocular tissue, in particular retinal layer thickness, which can give insight into pathological conditions such as glaucoma. The acquired 3D images were analyzed for the diameter of the blood vessel in the same axis location and the data was statically analyzed. The average diameter of retinal blood vessel in the left (control) eye was 0.012 micron, whereas in the right (treated) eye it was 0.025 micron ( $p < 0.0001$ ). This shows an approximately 100% increase in the diameter of the blood vessel in the treated vs. untreated eye. Other studies have established that the vessel diameters decreased significantly with increasing glaucoma stage independently of the patients' age. It is worth noting that application of the treatment in the right eye did not influence the diameter on the left eye, indicating a local and not systemic effect of the drug.

#### Regulatory Perspectives and Clinical Development for INM-085 for Glaucoma

As glaucoma is a common non-life-threatening disorder (affecting an estimated 2.8 million people in the United States) and as INM-085 is expected/intended to be a chronic therapy (daily dosing), this program will require comprehensive preclinical and clinical testing. For example, according to the International Conference on Harmonisation, or ICH,

guideline M3(2R), repeated-dose toxicity studies of six months in a rodent species and nine months in a non-rodent species will be required before studies in humans can be conducted with six months or more of treatment.

Regulatory agencies will expect careful and thorough investigation of minimally effective dose levels to ensure that upon approval the millions of patients who may be exposed to a new therapy will get enough drug to treat the disorder successfully, without complications from having received too much drug. Therefore, multiple Phase I and II studies are typically required in humans to investigate dose response with respect to both efficacy and safety.

Another ICH guideline, E1, outlines the size of the human safety database needed to support approval of chronic therapies for non-life-threatening conditions. Generally, the safety database should include data for at least 1,500 patients who have been exposed to the new therapy, with at least one year of drug treatment in a minimum of 100 patients. The required duration of treatment and follow-up for any particular new therapy may go well beyond this minimal ICH requirement, depending on the nature of adverse reactions observed in early Phase I and II clinical studies. For example, for the class of drugs called prostaglandin analogs, regulatory agencies required more than three years of follow-up to understand if certain adverse reactions (change in iris colour and changes in eyelashes) resolved after discontinuation of the medication. Drugs in a new class will generally need long Phase III studies in humans, lasting up to one to two years.

#### Key Milestones:

- May 10, 2017 – InMed announced the filing of a patent (US62/503,258) entitled, “Ocular Drug Delivery Formulation” for INM-085 as a cannabinoid-based topical (hydrogel) therapy for glaucoma, which is an important step in providing intellectual and commercial protection for this therapy. InMed is developing a stimulus-responsive, nanoparticle-laden vehicle for controlled delivery of ophthalmic drugs into the aqueous humor of the eye. The first applications of this vehicle will be for INM-085 as a cannabinoid-based topical therapy to reduce the intraocular pressure associated with glaucoma. INM-085 is intended for application as a once-per-day eye drop administered immediately prior to the patient's bedtime, intending to assist in reducing the high rate of non-adherence with current glaucoma therapies. Additionally, this novel, proprietary delivery system for ophthalmic drugs may also play an important role in enabling other companies' proprietary ophthalmic drug candidates or re-invigorating the commercial potential of off-patent products that would benefit from a once-a-day dosing regimen. InMed plans to initiate discussion with potential partners to this end.
- October 24, 2017 - InMed announced results from a study co-sponsored by InMed (Dr. Sazzad Hossain, Chief Scientific Officer) and University of British Columbia (laboratories of Professors Vikramaditya Yadav and Ujendra Kumar). The Company believes that the InMed-UBC study is the first ever to report hydrogel-mediated cannabinoid nanoparticle delivery into the eye, resulting in enhanced drug uptake via the cornea and lens. This study further evidences the Company's capacity to conduct a wide spectrum of drug development activities, including:
  - biosynthesis of a cannabinoid using a proprietary *E. coli*-based system;
  - packaging the cannabinoid as a nanoparticle;
  - formulation of a cannabinoid drug candidate into a novel, tissue specific delivery vehicle; and
  - confirmation of drug delivery and diffusion into a target tissue.

In this study, InMed's proprietary hydrogel delivery method offers unique rheological characteristics permitting it to form a thin, uniform coating, a 'gel-like lens', over the cornea through blinking of the eyelid. This lens holds the drug in place and allows for trans-corneal absorption of the drug, which can then diffuse within the eye to the retina. Total drug delivered using this hydrogel nanoparticle formulation was three-times higher than the control formulation.

- March 6, 2018 – InMed announced the publication of data on its glaucoma / hydrogel formulation program in the peer-reviewed journal Drug Delivery and Translational Research. The article, titled “A stimulus-responsive, in situ forming, nanoparticle-laden hydrogel for ocular drug delivery”, presents results from pre-clinical studies co-sponsored by InMed and was co-authored by Dr. Sazzad Hossain, InMed's Chief Scientific Officer and conducted at the labs of Drs. Vikramaditya Yadav and Ujendra Kumar at the University of British Columbia. In these studies, the investigators successfully validated the efficient transport of the formulated product in whole-eye experiments. The work seamlessly combined product design, synthetic biology,

polymer rheology, and analysis of mass transport within ocular tissue. The hydrogel was formulated as a composite of hyaluronic acid (HA) and methylcellulose (MC). Both polymers are biocompatible and highly muco-adhesive, making them ideal candidates for an ocular formulation. The amphiphilic nanoparticles were composed of a block copolymer composed of poly-ethylene oxide (PEO) and poly-lactic acid (PLA), designed to facilitate enhanced cannabinoid drug delivery into the eye via the cornea. For this study, the non-psychoactive cannabinoid cannabigerolic acid (CBGA) was biosynthesized using InMed's proprietary *E. coli*-based manufacturing approach. Results from the experiment verified the performance of a stimulus-responsive switching between thixotropy (thinning of the gel upon a shearing force, such as blinking) and temperature-dependent rheoexy (reforming as a gel after blinking), resulting in a thin, uniform gel-like lens that holds the drug in place to allow for transcorneal transport. Envisioned as a once-per-day (at bedtime) administration, this formulation is designed to address many of the issues associated with current glaucoma medications.

- May 14, 2018 – InMed announced the filing of a PCT patent application for the INM-085, a cannabinoid-based topical therapy for glaucoma, which includes protection of its technology in about 150 different countries including the USA, and claims a priority date from May 8, 2018 (PCT/CA2018/050548). The PCT filing is a conversion from the provisional patent filed in May 2017.

### **3.c. INM-405 in Pain**

According to an Institute of Medicine Report: *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research*, pain is a significant public health problem that is estimated to have an economic cost in the United States of at least \$560-\$635 billion annually. This includes estimated total incremental costs of pain-related healthcare ranging from \$261 to \$300 billion and \$297-\$336 billion due to lost productivity. According to the American Academy of Pain Medicine's "AAPM Facts and Figures on Pain", chronic pain affects far more Americans (est. 100 million) than diabetes (est. 26 million), coronary heart disease (est. 16 million) and cancer (est. 15 million) combined. The global pain management market for pharmaceuticals and medical devices is estimated to exceed \$36 billion in 2017, according to an August 2017 report from BCC Research.

Chronic pain can be categorized as either nociceptive (such as muscle pain), neuropathic (nerve pain such as pinched nerves in the lower back), and psychogenic pain (such as fibromyalgia). Each has different sensations, origins and potential treatment modalities. Other categories of pain include breakthrough pain, phantom pain, incident pain and others. Acute pain may follow any one of these categories.

Nociceptive pain is caused by stimulation of sensory nerve fibers that respond to stimuli approaching or exceeding harmful intensity (nociceptors), and may be classified according to the mode of noxious stimulation. The most common categories are "thermal" (e.g. heat or cold), "mechanical" (e.g. crushing, tearing, shearing, etc.) and "chemical" (e.g. iodine in a cut or chemicals released during inflammation).

Neuropathic pain is caused by damage or disease affecting any part of the nervous system involved in bodily feelings (the somatosensory system). Peripheral neuropathic pain is often described as "burning", "tingling", "electrical", "stabbing", or "pins and needles". Bumping the "funny bone" elicits acute peripheral neuropathic pain.

Psychogenic pain, also called psychalgia or somatoform pain, is pain caused, increased, or prolonged by mental, emotional, or behavioral factors. Headache, back pain, and stomach pain are sometimes diagnosed as psychogenic. Sufferers are often stigmatized, because both medical professionals and the general public tend to think that pain from a psychological source is not "real". However, specialists consider that it is no less actual or hurtful than pain from any other source.

According to a September 2016 fact sheet from the International Association for the Study of Pain, one type of chronic pain that may lend itself well to topical therapy is a set of neuropathic pain called orofacial pain, in particular TMD and trigeminal neuralgia, or TN. Both conditions are rooted in the trigeminal nerve that service the head and eyes (see Figure #3 below, 'ophthalmic nerve', 1), the cheek/upper lip (maxillary, 2) and the side of the face/mandible joint/jaw (mandibular, 3). Orofacial is common and has many causes. Several orofacial pain types are attributed to mechanical or neural injury near the surface of the skin, and this includes TMD and TN.

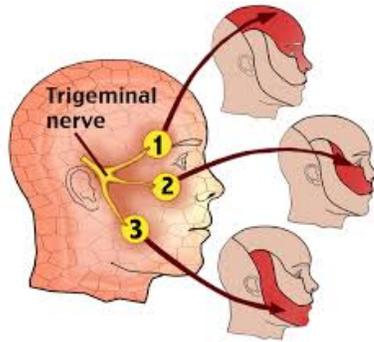


Figure #3 Trigeminal Neuralgia etiology

Source [www.trigeminal-neuralgia-therapy.com](http://www.trigeminal-neuralgia-therapy.com)

TMD encompasses a group of musculoskeletal and neuromuscular conditions involving the temporomandibular joint, or TMJ, masticatory muscles, and associated tissues. TMD pain can be associated with biomechanical dysfunction of the TMJ. TMD-related facial pain has been reported in 5-12% of the general population (with a female:male ratio of 2:1), according to the National Institute of Neurological Disorders and Stroke's fact sheet on trigeminal neuralgia, but only 4%-7% seek treatment. While often mild in nature, progression to severe and/or chronic pain is associated with greater stress and comorbidities and often results in significant loss of work and increase in other healthcare related costs. Typical pharmaceutical interventions include oral (systemic) NSAIDs such as ibuprofen and low-dose antidepressants.

In contrast, TN can be much more severe. TN is a unilateral painful disorder that is characterized by brief, electric-shock-like pain and is abrupt in onset and termination. TN originates at the stem prior to the nerve dividing into the three individual nerves and thus can affect the entire orofacial region. TN is a rare disease and studies on prevalence are scarce. According to a May 2005 publication from Manzoni *et al* titled "Epidemiology of typical and atypical craniofacial neuralgias", data suggest that TN has an incidence in the general population of between 4 to 5 per 100,000 people but some estimates range as high as 20 per 100,000 people in persons over 60 years of age. The ratio of women:men is 3:2, with a higher proportion seeing onset after the age of 40 and a higher incidence in patients with multiple sclerosis. Depending on severity and frequency, various surgical interventions are common. Typical pharmaceutical interventions include the anticonvulsant carbamazepine, although use of botulinum toxin to block nerve sensation and opioids to numb severe pain are common.

Osteoarthritis is a disease that damages the slippery tissue that covers the ends of bones in a joint. This allows bones to rub together. The rubbing causes pain, swelling, and loss of motion of the joint. Over time, the joint may lose its normal shape. The condition can cause bone spurs to grow on the edges of the joint. Bits of bone or cartilage can break off and float inside the joint space, which causes more pain and damage. According to information available on the National Institute of Arthritis and Musculoskeletal and Skin Diseases website, unlike some other forms of arthritis, osteoarthritis affects only joints and not internal organs.

Osteoarthritis is the most common type of arthritis. As reported in one study by Zhang *et al* in a paper titled "Epidemiology of Osteoarthritis", in patients > 26 years of age, symptomatic hand and knee osteoarthritis was reported in 6.8% and 4.9% of the study population, respectively. Another study cited an incidence of 100 per 100,000 for hand and 240 per 100,000 for knee. The Arthritis Foundation of America estimates that osteoarthritis affects more than 30 million persons in the USA, of which 14 million are knee osteoarthritis. Osteoarthritis is expected to impact over 130 million individuals worldwide by 2050.

A 2016 market report published by Credence Research, Inc. entitled "Global Osteoarthritis Treatment Market - Growth, Share, Opportunities, Pipeline Analysis, Competitive Analysis, and Forecast, 2016 - 2022," valued the global osteoarthritis treatment market at \$5 billion in 2015.

Current treatment for osteoarthritis include pain and anti-inflammatory medications in the form of pills, syrups, creams or lotions, or they are injected into a joint. According to the Arthritis Foundation, they include:

- Analgesics. These are pain relievers and include acetaminophen, opioids (narcotics) and an atypical opioid called tramadol. They are available over-the-counter or by prescription.
- NSAIDs. These are the most commonly used drugs to ease inflammation and related pain. NSAIDs include aspirin, ibuprofen, naproxen and celecoxib. They are available over-the-counter or by prescription.

- Corticosteroids. Corticosteroids are powerful anti-inflammatory medicines. They are taken by mouth or injected directly into a joint at a doctor's office.
- Hyaluronic acid. Hyaluronic acid occurs naturally in joint fluid, acting as a shock absorber and lubricant. However, the acid appears to break down in people with osteoarthritis. The injections are done in a doctor's office.

While there are numerous pharmaceutical products to treat various forms of both acute and chronic pain, the increase in the number of prescriptions for the opioid class of products (oxycodone, hydrocodone, morphine, methadone, fentanyl, etc.) has led to concerns as these products can be highly addictive and have damaging side effects, including death. According to the United States Centers for Disease Control and Prevention ('CDC'), drug overdose deaths and opioid-involved deaths continue to increase in the United States, with the majority (more than 60%) involving an opioid. Since 1999, the number of overdose deaths involving opioids (including prescription opioids and heroin) quadrupled, as have the number of prescriptions for opioids, yet there has been no increase in the amount of pain reported in the general population. From 2000 to 2015 more than half a million people died from drug overdoses. Thus, there is a need to find alternatives to treat chronic and severe pain that are non-addictive and have limited side effects.

There is a need to find alternatives to treat chronic and severe pain that are non-addictive and have limited side effects. InMed continues to research the potential of non-THC cannabinoids to treat pain using a topical formulation. Recently, InMed filed a provisional patent application in the United States for INM-405 and other unique compositions as cannabinoid-based topical therapies for the treatment of pain, which is an important step in protecting the Company's intellectual and commercial property. The foundation of this patent is the unreported data, cited above, on non-THC cannabinoids and their ability to modulate pain. The patent cites a range of cannabinoids, alone or in combination, applied topically to treat various types of pain - muscle, nerve, arthritis-induced joint pain, etc.

#### Key *in vivo* results for InMed's Pain Program:

Important data from InMed's development program for pain medications were published in in a 2017 European Journal of Pain article by Cairns *et al* titled "Delta-9-THC decreases masticatory muscle sensitization in female rats through peripheral cannabinoid receptor activation". While this publication specifically cited data on the use of THC, the Company has conducted similar research with other non-THC cannabinoids, alone and in combination at varying ratios, in similar study designs. Specifics on the non-THC data will not be made available unless and until the requisite patents have been filed and the data has been published in a peer-reviewed journal. Findings from the published study include:

- Expression of cannabinoid receptors on masseter ganglion neurons. Both CB1 and CB2 receptor expression was observed in the trigeminal ganglion neurons that innervate the masseter muscle, as well as in the neuronal fibers in the muscle itself. This confirms that these peripheral nerves may be appropriate targets for a cannabinoid therapy.
- Effect of intramuscular injections on THC on NGF-induced sensitization. NGF, if injected into a target tissue (muscle), makes the tissue more sensitive to pain, as can be measured by a mechanical threshold, or MT, scale. On this scale, a lower number represent a lower pain threshold, or a lower ability to tolerate a painful stimulus. NGF injection resulted in a lowering of the MT score. Application of THC (in this reported data) was associated with an increase of MT, meaning a higher ability to tolerate pain. It should be noted that the NGF-induced reduction in MT model mimics the type of pain reported by sufferers of TMD. Importantly, the THC only affected the muscle into which it was injected; there was no effect on surrounding tissue.
- In a behavioral analysis in this study, animals treated with peripheral application of THC, the leading psychoactive component in marijuana, did not exhibit any effect on motor function. This indicates that THC did not achieve sufficient circulatory distribution to reach the brain where it may exhibit psychoactivity.

#### Key Milestones

In 2014, the Company announced an additional therapy which was a proprietary mixture of cannabinoids and non-cannabis based active ingredients designed for the relief of joint pain and swelling associated with arthritis and joint disease. This program has since led to the following announcements:

- March 18, 2015 – InMed announced that it had initiated a program to identify and evaluate cannabinoid compounds for the treatment of chronic orofacial pain. Initial drug discovery and preclinical development continues in collaboration with members of the Faculty of Pharmaceutical Sciences at UBC. The work is being funded by a \$65,000 grant from Mitacs. Under the terms of its Mitacs-related grant to perform research at University of British Columbia facilities, InMed owns the intellectual property in the research results, excluding any intellectual property covered under separate agreement by UBC or InMed, any third party intellectual property used in the research, or any copyrighted material generated by the research team in performance of the project. Under the terms of the Mitacs program, InMed grants each of UBC, the academic supervisor, and the intern/fellow a royalty-free, non-exclusive, perpetual, irrevocable license to use the results for the purpose of carrying out the project and for research, scholarly publication, educational or other non-commercial use.
- August 20, 2015 – InMed announced the successful completion and validation of preclinical pain modelling, noting that InMed had successfully screened different cannabinoid compounds in *in vivo* electrophysiology and *in vivo* behavioural models of NGF induced pain.
- July 27, 2017 – InMed announced the publication of company-sponsored research in the European Journal of Pain. The article, titled “Delta-9-tetrahydrocannabinol decreases masticatory muscle sensitization in female rats through peripheral cannabinoid receptor activation”, presents results from a study co-sponsored by InMed and the MITACS Elevate Postdoctoral Fellowship program. The study was conducted by Dr. Hayes Wong and Prof. Brian Cairns at the University of British Columbia and was co-authored by Dr. Sazzad Hossain, Chief Scientific Officer of InMed. The study results suggest that peripheral application of cannabinoids targeting the natural endocannabinoid receptor system (in this case, receptor CB1) may provide a valuable approach in treating severe pain. The model utilized in this study mimics muscle pain reported by sufferers of TMD that affect the jaw muscles and joint.
- October 3, 2017 – InMed announced the filing of a provisional patent application entitled “Methods and Composition for Treatment of Pain with Cannabinoids”, in the United States (#62/562,166) for INM-405, a combination of non-THC cannabinoids, and other unique compositions as cannabinoid-based topical therapies for the treatment of pain, which is an important step in protecting the company's intellectual and commercial property.
- October 17, 2017 – InMed announced additional pre-clinical results in the development of INM-405 for the treatment of pain. In recent pre-clinical testing, InMed employed several methods to verify the effects of individual, non-THC (tetrahydrocannabinol, the primary psychoactive ingredient in cannabis) cannabinoids, as well as a matrix of cannabinoid combinations, delivered to treat peripheral pain:
  1. *in vivo* animal models of pain to measure the pain tolerance;
  2. *in vivo* electrophysiology recordings to measure the blockage of pain signal transmission in the peripheral nerve fibres; and
  3. *in vivo* behavioral studies to verify the CNS related side effects.Results from these studies suggest that peripheral application of certain cannabinoid compounds, alone or in combination, is effective in the treatment of craniofacial muscle pain disorders, without any observed CNS side effects, and may be a more desirable strategy than systemic pain-relief administration.

#### **4. Hydrogel formulation for once-a-day eye drops**

Cannabinoids are lipophilic in nature and we believe that with a novel delivery system, the reduction of IOP in glaucoma patients by topical (eye drop) application of cannabinoids will hold significant promise as a new therapy.

Current limitations of existing eye drop formulations include:

- Wiping away of the drops immediately after administration by blinking, leading to
- Inadequate drug exposure time to the surface of the eye, leading to
- Significant reduction in the amount of drug reaching its target.

Thus, the end result is the need for multiple administrations of the drug over the course of the day. Improvements are needed in drug delivery / formulations to address this.

As reported by Gaudana et al in their 2009 publication “Recent perspectives in ocular drug delivery”, colloidal dosage forms have been widely studied and employed in the field of ocular drug delivery. These dosage forms include liposomes, nanoparticles, microemulsions and nanoemulsions etc. Barriers to ocular drug delivery have already been described earlier in the context of structure and function of various ocular tissues and how each tissue can act as a barrier. The chronic nature of many ocular diseases necessitates frequent drug administration.

Advantages of colloidal dosage forms include:

- sustained and controlled release of the drug at the targeted site;
- reduced frequency of administration;
- ability to overcome blood–ocular barriers; and
- efflux-related issues associated with the parent drug.

Further, these carriers can also bypass or overcome various stability-related problems of drug molecules, e.g., proteins and peptides. Designing an ideal delivery system for any ocular disease depends on molecular properties of the drug such as size, charge, and affinity towards various ocular tissues and pigments.

InMed is developing a stimulus-responsive, nanoparticle-laden hydrogel vehicle for spatiotemporal and dosage-controlled release of cannabinoids into the aqueous humor of the eye. This hydrogel is envisioned to be packaged as a liquid and is intended for application as a once-per-day eye drop administered immediately prior to the patient’s bedtime. The liquid forms a gel when it reaches body temperature. Formulation of the product as a liquid permits easy dosing and simplifies the path towards development of a regulated, industrial-scale manufacturing process.

Key design criteria for InMed’s nanoparticle hydrogel include:

- Biocompatibility and biodegradability;
- Viscous fluid behavior while inside the container (to facilitate ease of manufacturing, handling and dosing);
- 4-6 hour drug release, absorption and subsequent carrier degradation;
- Triggered gel formation on the surface of the eye (to enhance pre-corneal residence time);
- Modulate the interplay between temperature-dependent rheopecty (becoming a **thicker** gel if influenced by temperature) and thixotrophy (becoming **thinner** liquid if a force is exerted, such as blinking);
- Optimized particle size and surface charge to avoid scratchy feelings inside the eye, enhance shelf-life, and to facilitate ocular penetration; and
- Muco-adhesive properties.

## **5. Other Research and Development Programs**

InMed has conducted a broad range of R&D activities to explore other uses of cannabinoids in treating human diseases with unmet medical needs. These programs are at various early stages of development and, as non-core assets, their continued development is subject to available resources and/or our ability to find funding partners. Continued investment in each program is under review and we will make determinations as to which programs to continue based on several strategic factors. In addition, we may choose to partner some or all of these programs with external parties.

### **5.1 Chronic Obstructive Pulmonary Disease, or COPD**

Chronic Obstructive Pulmonary Disease is a lung disease that includes chronic bronchitis and emphysema. According to the Canadian Lung Association, in 80-90% of cases, it is caused by smoking. Other causes of COPD can include:

- a. genetic reasons (alpha-1 antitrypsin deficiency);
- b. occupational dusts and chemicals;
- c. second hand smoke;
- d. frequent lung infections as a child; and

- e. wood smoke and other biomass (animal dung, crop residues) fuel used for cooking.

COPD develops over time. In most cases, COPD is diagnosed in people over 40 years of age. Someone with COPD may not realize that they are becoming more short of breath until it becomes very hard to do simple tasks like walking up stairs. When you have COPD, your lungs are obstructed or blocked, making it hard to breathe. In chronic bronchitis, your airways become swollen and can be filled with mucus, which can make it hard for you to breathe. In emphysema, the air sacs (alveoli) in your lungs are damaged which can make it hard for you to breathe.

According to World Health Organization estimates, 65 million people have moderate to severe COPD. More than 3 million people died of COPD in 2005, which corresponds to 5% of all deaths globally. Most of the information available on COPD prevalence, morbidity and mortality comes from high-income countries. Even in those countries, accurate epidemiologic data on COPD are difficult and expensive to collect. It is known that almost 90% of COPD deaths occur in low- and middle-income countries.

COPD can't be cured, but it can be treated. Early diagnosis, lifestyle changes and appropriate drug treatments can help you lead a normal and active life, feel better and stay out of hospital. There are several different therapies to treat COPD including bronchodilators, corticosteroids, antibiotics, and supplemental oxygen, among others.

The Company initiated a program to identify and evaluate cannabinoid compounds for the treatment of COPD using its bioinformatics platform. Initial drug discovery and preclinical development was completed in collaboration with members of the Department of Anesthesiology, Pharmacology & Therapeutics at UBC. Pursuant to the terms of the April 28, 2015 service contract with UBC that covers this project, all new intellectual property derived from this program is the sole property of InMed. Data from this research shows that, using *in vitro* assays using human lung fibroblasts (HFL-1 cell line), certain cannabinoid compounds are capable of affecting a specific protein in the biochemical pathway relevant to healing and fibrosis in the lung.

## 5.2 Neurodegenerative Diseases: Huntington's Disease

According to the Huntington's Disease Foundation, Huntington's disease is an inherited brain disorder. Huntington's disease causes cells in parts of the brain to die: specifically, the caudate, the putamen and, as the disease progresses, the cerebral cortex. As the brain cells die, a person with Huntington's becomes less able to control movements, recall events, make decisions and control emotions. The disease leads to incapacitation and, eventually, death (generally due to other health complications).

Huntington disease is a genetic disorder. The Huntington's disease gene is dominant, which means that each child of a parent with Huntington's disease has a 50% chance of inheriting the disease and is said to be "at-risk". Males and females have the same risk of inheriting the disease. Huntington's occurs in all races. Symptoms usually appear between the ages of 30 and 50, but the disease can appear in children or seniors. Huntington's disease affects an estimated 3 to 7 per 100,000 people of European ancestry. The disorder appears to be less common in some other populations, including people of Japanese, Chinese, and African descent.

At this time, there is no cure for Huntington's Disease. Researchers are working on a number of treatments that may slow down the progression of the disease. There are a number of interventions available today that improve the quality of life for Huntington's Disease sufferers.

Cannabinoids are a potentially rich yet largely under-exploited source of neuroprotective molecules. Neurodegenerative diseases incur high caregiver costs and diminish the economic output of societies. Since there are no known treatments for these diseases, discovering drugs that reverse or limit neurodegeneration is a medical priority. We focused our investigations on the treatment of Huntington's disease.

According to S. Frank's 2014 publication "Treatment of Huntington's disease", Huntington's disease is caused by a polyglutamine repeat in the huntingtin protein and is associated with severe atrophy in the striatum and cortex. In Huntington's disease, the loss of projection neurons in striatum is believed to be a classical pathology of disease. The leading cause of striatal atrophy is the nuclear inclusion of mutated huntingtin protein, or mHtt. As documented in multiple publications, the neuronal cell death due to mHtt linked to three well-articulated events including

activation of NMDA receptor, increased Ca<sup>2+</sup> influx and impaired mitochondrial. In the central nervous system, cannabinoid receptors are physiological regulators in cortical, striatal, limbic and hypothalamic neurons, according to Fernández-Ruiz *et al's* 2015 publication “Endocannabinoids and Neurodegenerative Disorders: Parkinson’s Disease, Huntington’s Chorea, Alzheimer’s Disease, and Others”. The biological effects of cannabis are mediated by signaling through a family of two receptor subtypes namely cannabinoid receptor 1 and 2, or CB1 and CB2. Several previous studies have demonstrated that CB1 is primarily confined in brain whereas CB2 expression is restricted to peripheral system. However, this concept has evolved as CB2 receptors are also present in central nervous system. Endocannabinoids are implicated in the pathophysiology of several diseases, e.g. Alzheimer’s, Parkinson’s and Huntington’s disease, inflammation, and epilepsy. According to Fernández-Ruiz *et al's* 2015 publication “Cannabinoids in neurodegeneration and neuroprotection”, the application of cannabinoids acts as an important contributing factor in neuroprotection and/or predisposition to glutamate-induced neurotoxicity. The overall goal of InMed’s research was to elucidate the mechanism for the neuroprotective role of cannabinoids in excitotoxicity.

We have screened seven cannabinoid compounds for their role in neuroprotection in an *in vitro* culture model of Huntington’s disease. Based on *in vitro* screening assays, we have established three different molecular targets that can be used to screen the repertoire of phytocannabinoids in an efficient manner. Published studies and our preliminary data support the hypothesis that cannabinoids via endocannabinoid receptors play a significant role in ameliorating neurotoxicity in Huntington’s disease. Pursuant to the terms of the March 2, 2015 service contract with UBC that covers this project, all new intellectual property derived from this program is the sole property of InMed.

### 5.3 Breast Cancer

The pathology of breast cancer is highly complicated and heterogeneous. Treatment failure and tumor progression in many cancers, including breast cancer, is associated with the development of drug-resistant tumor cell clones caused by genetic mutations in the malignant cells after treatment, according to S. Crawford’s 2013 article titled “Is it time for a new paradigm for systemic cancer treatment? Lessons from a century of cancer chemotherapy”.

InMed set out to determine the role of cannabinoids and the endocannabinoid receptors in modulation of signaling pathways associated with tumor progression and suppression in research conducted at UBC. Pursuant to the terms of the March 2, 2015 service contract with UBC that covers this project, all new intellectual property derived from this program is the sole property of InMed. Key research findings from this program include:

- We established the functional association between cannabinoids and breast cancer by determining the cannabinoid receptor expression in tumor cells.
- We established that cannabinoid receptors constitute a novel therapeutic target for breast cancer *in vitro*.

### **Intellectual Property – Patents and Know-how**

A patent is a monopoly granted by a government for a period of up to 20 years. A patent provides an enforceable legal right to prevent others from exploiting an invention being a product, device, system, substance, process or method in the country of grant. For an invention to be patentable, it must be novel, involve an inventive step (not obvious) and useful at the time of filing the initial patent application for that invention. At 18 months from the initial patent application, the detailed description of the invention is published. In order to secure patent protection, a patent application is filed with the patent office in each country of interest, the application is considered under the patent laws of that country, and a patent will issue if the application meets the patentability criteria of that country. After a patent expires or lapses, anyone can then use the invention.

The grant of a patent does not guarantee validity and a patent may be challenged by third parties at a patent office by re-examination in some countries or through the courts by revocation proceedings. The grant of a valid patent does not mean that the invention may be exploited in a given country without infringing third party intellectual property rights in that country.

The owner of a patent has the exclusive right to prevent others from making, selling, importing or otherwise using the patented invention for the life of the patent. Patent infringement occurs when someone makes, hires, uses, imports or

sells the patented invention, or a product made by a patented method, or offers to do these things, within the country covered by the patent without the permission of the owner of the patent.

Patent applications and patents are subject to payment of renewal fees over the life of the patent in order to maintain patent rights. If the renewal fees are not paid then the application or patent may lapse.

Adequate protection of intellectual property is a means to ensure that InMed can exploit its intellectual property and reduce the likelihood of imitation by competitors. InMed intends to utilize patents available to protect its IP wherever possible. While we cannot patent the naturally occurring individual cannabinoids used in our products, there are a number of other approaches to protect our inventions. These include:

- patents on combinations of cannabinoids that provide novel methods for treating diseases;
- formulations designed specifically to increase the safety and efficacy of drug treatments;
- cannabinoid delivery technology; and
- manufacturing processes for cannabinoids.

The patent methodologies listed above will be designed in a way to thoroughly protect InMed's multi-faceted approach to develop novel cannabinoid medicines. The Company does not intend to file for patent protection for its bioinformatics platform but instead plans, as noted earlier, to protect this asset as internal know-how.

#### **Manufacturing for INM-750, INM-085 and INM-405**

The APIs used in INM-750, INM-085 and INM-405 are currently sourced from either contract manufacturers or, for smaller quantities, from research material suppliers, that utilize either synthetic chemistry or extraction techniques from plant-based sources. This is intended to be an interim step to enable InMed to proceed with developing its formulation, execute preclinical toxicology studies and progress through Phase 1 and 2a clinical trials, after which time we anticipate that we will have been able to successfully scale up InMed's biosynthesis program so that it will be commercial-scale ready. Bridging studies consisting of chemical analysis and, possibly, animal bioavailability studies may be required in order to switch our API from the current external manufacturing sources to our internal biosynthesized products.

We expect that the final formulations (API + excipients + packaging) of INM-750 topical cream, the INM-085 eye drop formulation, and the INM-405 topical formulation will be manufactured by contract manufacturers and sub-component fabricators. The contract manufacturers and sub-component fabricators will be selected based on their specific competencies in manufacturing, quality standards, and materials. FDA regulations require that products be produced under current cGMPs.

#### **Grant Funding**

To date we have received approximately \$125,000 in Canadian federal grants which have provided us with funding and resources to continue the development of our product candidates and contributed to research and development efforts outside of our primary therapeutic focus. This grant funding has been received by our academic collaborators from Mitacs, a national, not-for-profit organization that accelerates innovative projects through strategic academic and industry collaboration in Canada, to support research related to INM-085 in glaucoma and our pain related programs. On September 11 2018, InMed announced that the University of British Columbia, laboratories of Prof. V. Yadav, was awarded a grant totaling \$136,000 over a three year period to off-set InMed's committed investment for the collaborative research and development project entitled "Microbial metabolic engineering for cannabinoid biosynthesis".

#### **Scientific Advisors**

InMed seeks external expertise to augment our internal abilities in all aspects of drug development in the form of consultants and scientific advisors. We are in the process of establishing a Scientific Advisory Board, or SAB, in the areas of cannabinoid science, formulation development, biosynthesis manufacturing and clinical practice for areas

related to our drug development programs. Currently, we have one individual formally appointed to our SAB:

Dr. Mauro Maccarrone, PhD - Scientific Advisor

Dr. Maccarrone is Professor and Chair of Biochemistry and Molecular Biology at Campus Bio-Medico, University of Rome. He also serves as Director of the Laboratory of Lipid Neurochemistry of the European Center for Brain Research-IRCCS Santa Lucia Foundation in Rome. Prof. Maccarrone served as the President of the International Cannabinoid Research Society and was the recipient of their 2016 Mechoulam Award. He also served as Chair of the 2015 Gordon Research Conference on Cannabinoid Function in the CNS, and is a founding member of the European Cannabinoid Research Alliance. In addition to having authored over 460 published papers, Dr. Maccarrone serves as referee or on the editorial boards to numerous scientific journals, including *Science*, *Nature Medicine*, *JAMA*, *PNAS*, *Blood*, *Brain*, *Journal of Neuroscience*, *Frontiers in Molecular Neuroscience*, *Cannabinoids and Cannabinoid Research*. He is also Editor of Biochemistry for the *Encyclopedia of Life Sciences*.

Dr. Vikramaditya Yadav, PhD – Scientific Advisor

Dr. Yadav is an Assistant Professor in the Department of Chemical & Biological Engineering and School of Biomedical Engineering at the University of British Columbia (UBC), and currently serves as the Chair of the Biotechnology Division of the Chemical Institute of Canada. He has been recognized by Medicine Maker journal as one of the 100 most influential people in drug development and manufacturing. Dr. Yadav received his Doctorate in Chemical Engineering from the Massachusetts Institute of Technology. His graduate work focused on enzyme and microbial metabolic engineering for the synthesis of pharmaceuticals. He later conducted post-doctoral research on biophysics and biological thermodynamics at Harvard University. He joined UBC, Canada's pre-eminent center for biotechnology research, in the summer of 2014 and has since established a world-leading, industry-connected research group that works on wide-ranging topics such as metagenomics, plant chemistry, tissue engineering, drug discovery and pharmaceutical manufacturing. Dr. Yadav received his Bachelor's Degree in Chemical Engineering from the University of Waterloo.

## **Facilities**

InMed currently outsources the majority of our research and development activities. We access lab space through existing service contracts at UBC in the Department of Pharmaceutical Sciences and The Department of Chemical and Biological Engineering. InMed's headquarters is a sub-leased office space in downtown Vancouver where the sub-lease expires August 31, 2019.

## **Employees**

We have a total of nine employees or dedicated consultants, four of whom are engaged on a full-time basis and five of whom are engaged on a less than full-time basis. Five of our employees are responsible for, and are engaged in activities related to, our research and development, planned clinical trials and regulatory affairs. Four of our employees/dedicated consultants are responsible for corporate and business development, administration, investor relations, accounting and finance. In addition to our permanent workforce, we regularly utilize outside consultants to provide advice on our basis R&D, clinical development planning, manufacturing/process development and preclinical research programs on a project-by-project basis. We have also engaged the services of three additional scientists under consulting agreements to execute on the lab-based experiments required to advance our technologies. These consultants have prior access to the requisite lab facilities and equipment for such experiments.

All of our employees and consultants have entered into non-disclosure and invention assignment agreements with us regarding our intellectual property, trade secrets and other confidential information. In addition, we have entered into non-competition agreements with each of our key employees and consultants. None of our employees are represented by a labor union or covered by a collective bargaining agreement, nor have we experienced any work stoppages.

## **Insurance**

We currently maintain director and officer insurance and property and general liability insurance. As our needs grow, we will secure insurance plans for the shipping and storage insurance for product candidates, clinical trial insurance, etc. We do not have key person insurance. If and when marketing approval is obtained for any of our product candidates, we will expand our insurance coverage to include the commercial sale of approved drug products.

## **DIVIDENDS**

No dividends have been paid by InMed on its Common Shares during its three most recently completed financial years. InMed may declare dividends in the future, depending on the financial requirements of the Company to finance future growth, InMed's financial condition and other factors which InMed's board of directors may consider appropriate in the circumstances. See "*Risk Factors*".

## **CAPITAL STRUCTURE**

### **Common Shares**

InMed's authorized share capital consists of an unlimited number of Common Shares without par value and an unlimited number of preferred shares without par value. As at June 30, 2018, InMed had 170,851,069 Common Shares issued and outstanding. As at the date of this AIF, InMed had 170,858,633 common shares issued and outstanding and no preferred shares issued and outstanding.

Each Common Share entitles the holder thereof to one vote at all meetings of shareholders. The shareholders are entitled to receive dividends, as and when declared by the board of directors of InMed, subject to the rights, privileges and restrictions attaching to the securities of InMed, which may be paid in money, property or by the issue of fully paid shares in the capital of InMed.

In the event of the liquidation, dissolution or winding-up of InMed, whether voluntary or involuntary, or other distribution of assets of InMed among shareholders for the purpose of winding up its affairs, subject to the rights, privileges and restrictions attaching to the securities of the Company, the shareholders shall be entitled to receive the remaining property of InMed. In the event of an insufficiency of property and assets to pay in full the amounts which the shareholders are entitled to receive upon such liquidation, dissolution or winding-up, the shareholders shall participate rateably among themselves in accordance with the amounts to which they are respectively entitled upon such liquidation, dissolution or winding-up.

### **Stock Options**

At the special meeting of the Company on March 24, 2017, the shareholders of InMed approved a new stock option plan. Pursuant to the plan, the board of directors of InMed may, from time to time, in its discretion and in accordance with the requirements of the CSE, grant to directors, officers, employees and consultants of InMed, non-transferable options to purchase Common Shares, provided that the number of Common Shares reserved for issuance will not exceed twenty percent (20%) of the issued and outstanding Common Shares at the date the options are granted (on a non-diluted and rolling basis). Stock options are exercisable on the date determined by the Compensation Committee and specified in the option agreement pursuant to which the stock option is granted. The new stock option plan also applies to all outstanding stock options of the Company that were granted prior to March 24, 2017 under the terms of the Company's prior stock option plan. For further details with respect to the Company's stock option plan see the information circular of the Company dated February 22, 2017 prepared in respect of the special meeting of the Company's shareholders held on March 24, 2017, a copy of which information circular has been filed under InMed's profile on SEDAR and is available at [www.sedar.com](http://www.sedar.com).

As at June 30, 2018, InMed had 17,095,000 options issued and outstanding with a weighted average exercise price of \$0.53 and a weighted average term to expiry of 3.67 years.

During the period from June 30, 2018 to the date of this AIF, a total of 270,000 options have been granted and 200,000 options have been cancelled.

As at the date of this AIF, InMed has 17,165,000 options issued and outstanding with a weighted average exercise price of \$0.52 and a weighted average term to expiry of 3.48 years.

### Share Purchase Warrants

As at June 30, 2018, InMed had 31,912,704 common share purchase warrants (“warrants”), issued and outstanding with a weighted average exercise price of \$1.21 per share. Each warrant entitles the holder thereof to purchase one Common Share. During the year ended June 30, 2018 InMed issued an additional 30,039,815 warrants which have an exercise price of \$1.25 per share. During the year ended June 30, 2018, 7,561,111 warrants were exercised at a weighted average exercise price of \$0.45 per Common Share purchased.

During the period from June 30, 2018 to the date of this AIF, a total of 35,000 warrants have been exercised. No warrants have been granted or expired in this period.

As at the date of this AIF, InMed has 31,877,704 warrants issued and outstanding with an exercise price of \$1.22 and which expire at various dates from May 31, 2019 to June 21, 2020. The warrants issued and outstanding as at the date of this AIF are comprised of the following:

- 1,837,889 warrants (the “May 2017 Warrants”) that were issued as part of InMed’s marketed underwritten offering of 12,788,000 units at a price of \$0.45 per unit that closed on May 31, 2017, or the May 2017 Offering;
- 13,428,571 warrants (the “January 2018 Warrants”) that were issued as part of InMed’s private placement of 13,428,571 units at a price of \$0.70 per unit that closed on January 3, 2018, or the January 2018 Offering; and
- 16,611,244 warrants (the “June 2018 Warrants”), that were issued as part of InMed’s bought deal financing 16,611,244 units at a price of \$0.90 per unit that closed on June 21, 2018, or the June 2018 Offering.

### May 2017 Warrants

The 1,837,889 outstanding May 2017 Warrants are governed by the terms of a warrant indenture (the “May 2017 Warrant Indenture”) dated May 31, 2017 between the Company and Computershare Trust Company of Canada, as the Warrant Agent. The following is a brief summary of the material attributes and characteristics of the warrants and certain principal provisions of the May 2017 Warrant Indenture. This summary does not purport to be complete and is subject to, and qualified in its entirety by reference to, the terms of the May 2017 Warrant Indenture, a copy of which has been filed and is available under the Company’s profile on SEDAR at [www.sedar.com](http://www.sedar.com).

Each whole warrant entitles the holder to acquire one Common Share (a “May 2017 Warrant Share”), at an exercise price of \$0.65 until 5:00 p.m. (Vancouver Time) on May 31, 2019, subject to adjustment in certain events, after which time the warrant will be void and of no value. May 2017 Warrants are only be exercisable on a net cashless basis based on the five-day volume-weighted average trading price of the Common Shares on the TSX ending on the date immediately preceding the date of exercise. Specifically, a warrant holder who duly exercises their May 2017 Warrants shall be entitled to receive that number of May 2017 Warrant Shares equal to the quotient obtained by dividing  $(A-B) \times X$  by A, where:

A = the volume weighted average trading price of the Common Shares on the TSX, for the five consecutive trading days immediately preceding the time of delivery of the exercise form giving rise to the applicable cashless exercise;

B = the exercise price of the May 2017 Warrant, as may be adjusted pursuant to the terms of the May 2017 Warrant Indenture; and

X = the number of May 2017 Warrant Shares that would be issuable upon exercise of the warrant in accordance with the terms of such warrant if such exercise were completed by means of a cash exercise rather than a cashless exercise.

The May 2017 Warrants and the May 2017 Warrant Shares have not been and will not be registered under the U.S. Securities Act of 1933, as amended, the (“U.S. Securities Act”), or any applicable state securities laws, and the

warrants may not be exercised unless an exemption or exclusion from such registration is available and documentation to that effect is provided in accordance with the terms of the May 2017 Warrant Indenture.

Other than May 2017 Warrants comprising part of the units resold pursuant to Rule 144A under the U.S. Securities Act, which were represented by definitive certificates in fully registered form, the May 2017 Warrants may be issued in uncertificated form. Any warrants issued in certificated form shall be evidenced by a warrant certificate in the form attached to the May 2017 Warrant Indenture. All May 2017 Warrants issued in the name of CDS & Co. may be in either a certificated or uncertificated form, such uncertificated form being evidenced by a book-entry position on the register of warrant holders to be maintained by the Warrant Agent at its principal offices in Vancouver, British Columbia.

The May 2017 Warrant Indenture provides that the share ratio and exercise price of the May 2017 Warrants are subject to adjustment in the event of a subdivision or consolidation of the Common Shares. The May 2017 Warrant Indenture also provides that if there is (a) a reclassification or change of the Common Shares, (b) any consolidation, amalgamation, arrangement or other business combination of the Company resulting in any reclassification, or change of its Common Shares into other shares, or (c) any sale, lease, exchange or transfer of the Company's assets as an entity or substantially as an entirety to another entity, then each holder of a May 2017 Warrant which is thereafter exercised shall receive, in lieu of Common Shares, the kind and number or amount of other securities or property which such holder would have been entitled to receive as a result of such event if such holder had exercised the May 2017 Warrants prior to the event.

No adjustment in the exercise price or number of May 2017 Warrant Shares will be required to be made unless the cumulative effect of such adjustment or adjustments would result in a change of at least 1% in the exercise price or a change in the number of May 2017 Warrant Shares purchasable upon exercise by at least one one-hundredth (1/100th) of a Common Share, as the case may be.

The May 2017 Warrant Indenture also provides that, during the period in which the May 2017 Warrants are exercisable, the Company will give notice to holders of May 2017 Warrants of certain stated events, including events that would result in an adjustment to the exercise price for the May 2017 Warrants or the number of May 2017 Warrant Shares issuable upon exercise of the May 2017 Warrants, at least 14 days prior to the record date or effective date, as the case may be, of such events.

From time to time, the Company and the Warrant Agent, without the consent of the holders of warrants, may amend or supplement the May 2017 Warrant Indenture for certain purposes, including curing defects or inconsistencies or making any change that does not adversely affect the rights of any holder of May 2017 Warrants. Any amendment or supplement to the May 2017 Warrant Indenture that adversely affects the interests of the holders of the May 2017 Warrants may only be made by "extraordinary resolution", which is defined in the May 2017 Warrant Indenture as a resolution either (1) passed at a meeting of the holders of May 2017 Warrants at which there are holders of warrants present in person or represented by proxy representing at least 20% of the aggregate number of the then outstanding May 2017 Warrants and passed by the affirmative vote of holders of May 2017 Warrants representing not less than 66 2/3% of the aggregate number of all the then outstanding May 2017 Warrants represented at the meeting and voted on the poll upon such resolution, or (2) adopted by an instrument in writing signed by the holders of not less than 66 2/3% of the aggregate number of all then outstanding May 2017 Warrants.

No fractional warrants will be issued and no fractional May 2017 Warrant Shares will be issuable upon the exercise of any May 2017 Warrants, and no cash or other consideration will be paid in lieu of fractional shares. Holders of May 2017 Warrants will not have any voting or pre-emptive rights or any other rights which a holder of Common Shares of the Company would have.

#### January 2018 Warrants

The 13,428,571 outstanding January 2018 Warrants are governed by the terms of warrant certificates, or the January 2018 Warrant Certificates, between the Company and each of the individual investors. The following is a brief summary of the material attributes and characteristics of the warrants and certain principal provisions of the January 2018 Warrant Certificates.

Each whole January 2018 Warrant entitles the holder to acquire one Common Share, a January 2018 Warrant Share, at a cash exercise price of \$1.25 until 4:00 p.m. (Vancouver Time) on July 3, 2019, subject to adjustment in certain events, after which time the January 2018 Warrant will be void and of no value.

The January 2018 Warrants are non-transferrable.

The January 2018 Warrants and the January 2018 Warrant Shares have not been and will not be registered under the U.S. Securities Act or any applicable state securities laws, and the January 2018 Warrants may not be exercised unless an exemption or exclusion from such registration is available and documentation to that effect is provided in accordance with the terms of the January 2018 Warrant Certificates.

The January 2018 Warrant Certificates provide that the share ratio and exercise price of the warrants are subject to adjustment in the event of a subdivision or consolidation of the Common Shares of the Company or the declaration of a stock dividend. The purchase price and number of Common Shares which the warrant holder is entitled are subject to adjustment in the event of an issuance to current holders of Common Shares of rights, options or warrants to purchase Common Shares of the Company or in the event of a distribution of (i) shares of any class, (ii) rights, options or warrants, (iii) evidence of its indebtedness, or (iv) certain other property or assets. The January 2018 Warrant Certificates also provide that if there is (a) a reclassification or change of the Common Shares of the Company, (b) any consolidation, amalgamation, or merger of the Company resulting in any reclassification, or change of its Common Shares into other shares, or (c) any sale of the Company's assets as an entity or substantially as an entirety to another entity, then each holder of a warrant which is thereafter exercised shall receive, in lieu of Common Shares of the Company, the kind and number or amount of other securities or property which such holder would have been entitled to receive as a result of such event if such holder had exercised the January 2018 Warrants prior to the event.

No fractional warrants will be issued and no fractional January 2018 Warrant Shares will be issuable upon the exercise of any January 2018 Warrants, and no cash or other consideration will be paid in lieu of fractional shares. Holders of January 2018 Warrants will not have any voting or pre-emptive rights or any other rights which a holder of Common Shares of the Company would have.

#### June 2018 Warrants

The 16,611,244 outstanding June 2018 Warrants are governed by the terms of a warrant indenture (the "June 2018 Warrant Indenture") dated June 21, 2018 between the Company and Computershare Trust Company of Canada, as the Warrant Agent. The following is a brief summary of the material attributes and characteristics of the June 2018 Warrants and certain principal provisions of the June 2018 Warrant Indenture. This summary does not purport to be complete and is subject to, and qualified in its entirety by reference to, the terms of the June 2018 Warrant Indenture, a copy of which has been filed and is available under the Company's profile on SEDAR at [www.sedar.com](http://www.sedar.com).

Each whole warrant entitles the holder to acquire one Common Share, a June 2018 Warrant Share, at a cash exercise price of \$1.25 until 5:00 p.m. (Vancouver Time) on June 21, 2020, subject to adjustment in certain events, after which time the June 2018 Warrant will be void and of no value.

The June 2018 Warrants are listed for trading on the TSX under the symbol IN.WT.

The June 2018 Warrants and the June 2018 Warrant Shares have not been and will not be registered under the U.S. Securities Act or any applicable state securities laws, and the warrants may not be exercised unless an exemption or exclusion from such registration is available and documentation to that effect is provided in accordance with the terms of the June 2018 Warrant Indenture.

The June 2018 Warrants may be issued in uncertificated form. Any June 2018 Warrants issued in certificated form shall be evidenced by a warrant certificate in the form attached to the June 2018 Warrant Indenture. All June 2018 Warrants issued in the name of CDS & Co. may be in either a certificated or uncertificated form, such uncertificated form being evidenced by a book-entry position on the register of warrant holders to be maintained by the Warrant Agent at its principal offices in Vancouver, British Columbia.

The June 2018 Warrant Indenture provides that the share ratio and exercise price of the June 2018 Warrants are subject to adjustment in the event of a subdivision or consolidation of the Common Shares of the Company. The June 2018 Warrant Indenture also provides that if there is (a) a reclassification or change of the Common Shares of the Company, (b) any consolidation, amalgamation, arrangement or other business combination of the Company resulting in any reclassification, or change of its Common Shares into other shares, or (c) any sale, lease, exchange or transfer of the Company's assets as an entity or substantially as an entirety to another entity, then each holder of a June 2018 Warrant which is thereafter exercised shall receive, in lieu of Common Shares of the Company, the kind and number or amount of other securities or property which such holder would have been entitled to receive as a result of such event if such holder had exercised the June 2018 Warrants prior to the event.

No adjustment in the exercise price or number of June 2018 Warrant Shares will be required to be made unless the cumulative effect of such adjustment or adjustments would result in a change of at least 1% in the exercise price or a change in the number of June 2018 Warrant Shares purchasable upon exercise by at least one one-hundredth (1/100th) of a Common Share of the Company, as the case may be.

The June 2018 Warrant Indenture also provides that, during the period in which the June 2018 Warrants are exercisable, the Company will give notice to holders of June 2018 Warrants of certain stated events, including events that would result in an adjustment to the exercise price for the warrants or the number of June 2018 Warrant Shares issuable upon exercise of the warrants, at least 14 days prior to the record date or effective date, as the case may be, of such events.

From time to time, the Company and the Warrant Agent, without the consent of the holders of June 2018 Warrants, may amend or supplement the June 2018 Warrant Indenture for certain purposes, including curing defects or inconsistencies or making any change that does not adversely affect the rights of any holder of June 2018 Warrants. Any amendment or supplement to the June 2018 Warrant Indenture that adversely affects the interests of the holders of the warrants may only be made by "extraordinary resolution", which is defined in the June 2018 Warrant Indenture as a resolution either (1) passed at a meeting of the holders of June 2018 Warrants at which there are holders of warrants present in person or represented by proxy representing at least 20% of the aggregate number of the then outstanding warrants and passed by the affirmative vote of holders of June 2018 Warrants representing not less than 66 2/3% of the aggregate number of all the then outstanding June 2018 Warrants represented at the meeting and voted on the poll upon such resolution, or (2) adopted by an instrument in writing signed by the holders of not less than 66 2/3% of the aggregate number of all then outstanding June 2018 Warrants.

No fractional warrants will be issued and no fractional June 2018 Warrant Shares will be issuable upon the exercise of any June 2018 Warrants, and no cash or other consideration will be paid in lieu of fractional shares. Holders of June 2018 Warrants will not have any voting or pre-emptive rights or any other rights which a holder of Common Shares of the Company would have.

### **Agent's Warrants**

As at June 30, 2018, InMed had 1,539,953 warrants that had been issued to agents issued and outstanding. Each agent's warrant entitles the holder thereof to purchase one Common Share. During the year ended June 30, 2018 InMed issued an additional 1,539,953 agent's warrants while 670,984 agent's warrants were exercised at a weighted average exercise price of \$0.40 per Common Share purchased.

From June 30, 2018 to the date of this AIF, no agent warrants have been exercised, granted or expired. As at the date of this AIF, InMed has 1,539,953 agent's warrants issued and outstanding with a weighted average exercise price of \$1.11 and a weighted average term to expiry of 1.50 years.

### **Constraints**

There are no constraints imposed on the ownership of securities of InMed to ensure a certain level of Canadian ownership of InMed.

## Ratings

InMed has not requested, nor to management's knowledge has InMed received, any ratings from any rating organizations in respect of any of InMed's securities.

## MARKET FOR SECURITIES

### Common Shares

The Common Shares currently trade under the symbol "IN" on the Toronto Stock Exchange. Prior to commencing trading on the Toronto Stock Exchange on March 26, 2018, the Common Shares traded on the Canadian Securities Exchange. The following tables set out the price range and trading volume of the Common Shares, as reported by the Toronto Stock Exchange, on both the Canadian Securities Exchange and the Toronto Stock Exchange for each month in InMed's financial year ended June 30, 2018, and the current fiscal year to date:

#### *Common Shares on the Canadian Securities Exchange*

Month	Common Shares Price Range		Total Volume
	High (\$)	Low (\$)	
July 2017	0.38	0.30	5,536,987
August 2017	0.33	0.23	7,047,281
September 2017	0.56	0.26	19,527,180
October 2017	0.53	0.36	12,611,005
November 2017	0.79	0.42	35,696,289
December 2017	1.46	0.66	47,447,850
January 2018	2.42	1.12	80,190,767
February 2018	1.30	0.68	20,936,148
March 1 – 25 2018	1.88	0.85	45,439,059

#### *Common Shares on the Toronto Stock Exchange*

Month	Common Shares Price Range		Total Volume
	High (\$)	Low (\$)	
March 26 – 31 2018	1.69	1.29	3,583,227
April 2018	1.42	1.08	7,126,316
May 2018	1.24	0.89	12,914,170
June 2018	1.14	0.72	18,388,227
July 2018	0.89	0.72	6,021,933
August 2018	0.90	0.66	9,736,060
September 1 – 12 2018	1.08	0.78	8,236,101

### June 2018 Warrants

The June 2018 Warrants currently trade under the symbol "IN.WT" on the Toronto Stock Exchange.

The following table sets out the price range and trading volume of the June 2018 Warrants, as reported by the Toronto Stock Exchange, on the Toronto Stock Exchange for the period June 21, 2018, when they commenced trading, until June 30, 2018 and the current fiscal year to date:

Month	June 2018 Warrants Price Range		Total Volume
	High (\$)	Low (\$)	
June 21 – 30, 2018	0.22	0.105	2,994,898
July 2018	0.20	0.15	1,103,958
August 2018	0.19	0.15	696,449
September 1 – 12, 2018	0.38	0.165	431,458

## Other Securities

No securities of InMed, other than Common Shares, have been issued since July 1, 2017, except as set out below.

## Options

The following table sets out the options issued by InMed since July 1, 2017:

Date of Issuance	Number of Options	Exercise Price	Expiry Date	Grant Date Fair Value
July 10, 2017	400,000	\$0.33	July 22, 2022	\$0.33
August 14, 2017	1,350,000	\$0.275	August 14, 2022	\$0.275
September 12, 2017	1,000,000	\$0.425	September 12, 2022	\$0.425
March 8, 2018	2,700,000	\$1.55	March 8, 2023	\$1.55
May 16, 2018	2,790,000	\$1.02	May 16, 2023	\$1.02
August 31, 2018	270,000	\$0.82	August 31, 2018	\$0.82

## Warrants

The following table sets out the Warrants issued by InMed since July 1, 2017:

Date of Issuance	Number of Warrants	Exercise Price	Expiry Date	Grant Date Fair Value
January 3, 2018	13,428,571	\$1.25 <sup>(1)</sup>	July 3, 2019	\$2.37 <sup>(1)</sup>
June 21, 2018	16,611,244	\$1.25	June 21, 2020	\$0.88

<sup>(1)</sup> The exercise price for the Warrants issued in connection with the closing of the private placement of the Company on January 3, 2018 was determined at the time the Company filed for price protection for the private placement. The Company's share price increased in the intervening time between filing for price protection and the closing of the private placement. Accordingly, the exercise price for the Warrants was below the market price of the Company's common shares at the time of closing of the private placement.

## Agent's Warrants

The following table sets out the agent's warrants issued by InMed since July 1, 2017:

Date of Issuance	Number of Agent's Warrants	Exercise Price	Expiry Date	Grant Date Fair Value
January 3, 2018	433,556	\$1.25 <sup>(1)</sup>	July 3, 2019	\$2.37 <sup>(1)</sup>
June 21, 2018	1,106,397	\$1.25	June 21, 2020	\$0.88

<sup>(1)</sup> The exercise price for the Warrants issued in connection with the closing of the private placement of the Company on January 3, 2018 was determined at the time the Company filed for price protection for the private placement. The Company's share price increased in the intervening time between filing for price protection and the closing of the private placement. Accordingly, the exercise price for the Warrants was below the market price of the Company's common shares at the time of closing of the private placement.

## ESCROWED SECURITIES

As at June 30, 2018, no outstanding Common Shares or other securities of InMed were held in escrow.

### DIRECTORS AND MANAGEMENT

The board of directors (each of whom has been appointed to hold office until the close of InMed’s next annual general meeting) and management of InMed currently consist of the following individuals:

<b>Name, Address of Residence and Position with InMed</b>	<b>Principal Occupation During the Last Five Years</b>	<b>Date of First Appointment as a Director or Officer</b>	<b>Number of InMed Securities Held</b>
ERIC A. ADAMS <sup>(1)(5)</sup> British Columbia, Canada President, CEO and Director	President and CEO of InMed (June 16, 2016–present); President, CEO (March 2004-May 2011) and Director of enGene Inc. (March 2004-July 2013); CEO of Ronin8 Technologies, Ltd. (November 2014-February 2015).	June 16, 2016	230,225 Common Shares 6,400,000 options 222,225 warrants
MARTIN BOTT <sup>(2)(3)(5)</sup> Indiana, USA Director	VP Finance, Special Projects (January 2018–present); VP Finance, Corporate Finance and Investment Banking (April 2015-December 2017); VP of Finance, CFO of Diabetes Business Unit and CFO Global Manufacturing and Quality (May 2011-March 2015), Eli Lilly & Company.	January 13, 2017	100,000 Common Shares 1,000,000 options
ADAM CUTLER <sup>(2)(3)(5)</sup> New York, USA Director	CFO of Molecular Templates, Inc. (November 2017–present); SVP, Corporate Affairs-Arbutus Biopharma (March 2015–November 2017); Managing Director, Trout Group Capital (June 2012 –February 2015); Director and Sr. Biotechnology Analyst, Credit Suisse (March 2011– June 2012).	November 23, 2015	1,000,000 options
WILLIAM J. GARNER, M.D. <sup>(2)(4)(5)</sup> Puerto Rico Director	EGB Advisors PR LLC. Founder and Chairman of Race Oncology (July 2016-present). Founder and Chairman of Isla Pharmaceuticals (March 2017-present). Co-founder and Director, DelMar Pharmaceuticals, Inc. (February 2013-January 2016). Founder, CEO of Invion (August 2012- May 2013).	June 13, 2016	800,000 options
ANDREW HULL <sup>(2)(3)(4)(5)</sup> Illinois, USA Director	Vice President of Global Alliances, Takeda Pharmaceuticals (April 2014-April 2018); VP, Global Alliance Management (June 2008–April 2014). Chairman, Illinois Biotechnology Industry Organization (2009, 2014, 2015).	September 12, 2016	625,000 Common Shares 1,000,000 options
JOSH BLACHER New York, USA Chief Business Officer	Chief Business Officer of InMed (April 2018–present); Chief Financial Officer of Therapix Biosciences Ltd. (April 2017–April 2018); Chief Financial Officer of Galmed Pharmaceuticals Ltd. (October 2014-March 2017); Executive Vice President, Corporate Development, Lifewatch Inc. (2011-2014).	April 9, 2018	1,375,000 options
JEFF CHARPENTIER British Columbia, Canada Chief Financial Officer	Chief Financial Officer of InMed (December 2016 – present); CFO, ImStar Therapeutics Inc. (July 2016 – present); CFO, Proactive Immune Sciences Corp. (October 2014-present); CFO, Lifebank Inc. (October 2010-February 2013); CFO, viDA Therapeutics Inc. (October 2011-February 2015)	December 15, 2016	850,000 options
SAZZAD HOSSAIN, PhD British Columbia, Canada Chief Scientific Officer	Chief Scientific Officer of InMed (May 2014–present); Group Leader and Head of Pharmacology, biotechnology Research Institute, National Research Council of Canada (October 2008–March 2014).	May 10, 2014	2,657,500 Common Shares 1,600,000 options
ERIC C. HSU, PhD British Columbia, Canada VP -Preclinical R&D	VP Preclinical R&D, InMed (March 2018–present); VP of Research and VP of Scientific Affairs and Operations, enGene Inc. (August 2002–March 2018).	March 13, 2018	845,000 options
ALEXANDRA D.J. MANCINI British Columbia, Canada SVP - Clinical and Regulatory Affairs	SVP, Clinical and Regulatory Affairs of InMed (October 2016–present); Founder and President, True North Synergy Inc. (September 1999-present); Senior VP, Clinical and Regulatory Affairs, Sirius Genomics Inc. (September 2008–September 2012).	October 31, 2016	1,000,000 options 50,000 warrants

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(1) Not an independent director under National Instrument 58-101 – *Disclosure of Corporate Governance Practices* because he is an executive officer of InMed.

(2) Independent director under National Instrument 58-101 – *Disclosure of Corporate Governance Practices*.

(3) Member of the Audit Committee.

(4) Member of the Compensation Committee.

(5) Member of the Nominating & Governance Committee.

Dr. Ado Muhammad, who has worked with InMed since March 2015 under the title Chief Medical Officer, has transitioned to the title of Sr. Consultant, Medical Affairs. While his role with and contribution to the Company remain essentially unchanged, he is no longer considered an executive officer of InMed.

## **Profile of the Board and Management**

### ***Eric A. Adams, President, CEO and Director***

Mr. Adams is a seasoned biopharmaceutical executive with over 30 years' experience in company and capital formation, global market development, mergers and acquisitions, licensing and corporate governance. Mr. Adams previously served as CEO at enGene Inc., which he led from a nascent start-up to becoming a venture capital-backed leader in gene therapy. Prior to enGene, he held key senior roles in global market development with QLT Inc. (Vancouver), Advanced Tissues Science Inc. (La Jolla), Abbott Laboratories (Chicago), and Fresenius AG (Germany). Mr. Adams is well regarded in the Canadian biotech industry for his service as a strategic advisor to a number of early-stage biotech companies, as a previous Chairman of BIOTECCanada's Emerging Company Advisory Board and for his extensive generosity in mentoring biotech entrepreneurs. He is a dual citizen of Canada and the United States and holds a Masters of International Business from the University of South Carolina and a Bachelors in Chemistry from the University of Southern Indiana.

### ***Martin Bott, Director***

Mr. Bott has over 30 years of experience in senior financial and executive leadership. He currently serves as VP Finance, Special Projects at Eli Lilly & Company. He joined Lilly in 1988 and has held roles of increasing responsibility at their headquarters in Indianapolis as well as affiliates in Switzerland, Germany, and the UK. Prior to his current assignment, Mr. Bott was leading the Corporate Finance and Investment Banking group since 2015 and, prior to this, was the CFO for both the Diabetes Business and the Global Manufacturing and Quality organizations. He has been a member of the Lilly CFO Staff since December 2002. Mr. Bott has a Bachelor degree in Business / Marketing (Cologne, Germany, 1985) and a Master's in International Business Studies (University of South Carolina, 1988).

### ***Adam Cutler, Director***

Mr. Cutler has over 20 years of experience in the global healthcare industry where he successfully held senior leadership positions in various roles from Equity Research, Corporate Affairs and Strategy, Investor Relations and Consulting. Mr. Cutler earned a reputation as a top-ranked biotechnology sell-side analyst and advisor, with extensive knowledge of biotech product development, the global healthcare environment, and the United States financial community. Mr. Cutler is currently Chief Financial Officer at Molecular Templates, Inc. Previously, he was Senior Vice President of Corporate Affairs at Arbutus Biopharma and, prior to that, was Managing Director at The Trout Group LLC and Trout Capital LLC, where he successfully executed financings and advised a wide range of life science companies on investor relations, business development, and capital raising strategy. Mr. Cutler spent almost 12 years as a sell-side analyst with firms including Credit Suisse, Canaccord Genuity, JMP Securities, and Bank of America Securities, with prior analytical and consulting experience at The Frankel Group and Ernst & Young, Healthcare Consulting. Mr. Cutler holds a BA in Economics from Brandeis University.

***William J. Garner, MD, Director, Chairman of the Board***

Dr. Garner is the founder of EGB Ventures, where he has focused on advancing technologies and companies to significant value inflection points, leading to monetization of assets via licensing, mergers and acquisitions or IPO transactions. Dr. Garner has extensive director-level and executive management experience, including his current appointment as Non-Executive Chairman & Founder of Race Oncology (ASX:RAC) and as Founder and Chairman at Isla Pharmaceuticals with a Dengue therapeutic; previously serving as CEO of Invion Limited, a clinical-stage anti-inflammatory drug development company that resulted from the merger of a private company he founded; and as a co-founder and Director of Del Mar Pharmaceuticals (NASDAQ:DMPI). Dr. Garner brings additional medical affairs experience from his tenure at Hoffmann LaRoche's oncology division. Prior to Roche, Dr. Garner was a healthcare merchant banker in New York City. He has a Master of Public Health from Harvard and earned his M.D. at New York Medical College. Dr. Garner did residency training in Anatomic Pathology at Columbia-Presbyterian and is currently a licensed physician in the State of New York.

***Andrew Hull, Director***

Mr. Hull has over 30 years' experience in various commercial and business development roles with leading pharmaceutical and biotech companies. He most recently served as Vice President of Global Alliances for Takeda Pharmaceuticals where he was responsible for maximizing the success of Takeda's growing number (40+) of commercial and R&D partnerships with many of the industry's leading pharmaceutical and biotech companies. In previous roles, he led marketing and commercial development of Takeda's United States portfolio of over \$3B including diabetes, neuroscience, GI and cardiovascular therapies. Additionally, he held positions of increasing responsibility at Immunex and Abbott Laboratories. Mr. Hull received a bachelor's degree in biology from Kenyon College in 1985. He also recently served as a member of the Board of Directors of the Illinois Biotechnology Industry Organization and recently was a member of the Kenyon College Board of Trustees.

***Josh Blacher, Chief Business Officer***

Mr. Blacher brings two decades of leadership experience in senior positions within the US healthcare and capital markets sectors, focusing primarily on strategic finance, business development, and managing relations with the investment community. Before joining InMed, Mr. Blacher served as Chief Financial Officer at Therapix Biosciences (NASDAQ:TRPX) and Galmed Pharmaceuticals (NASDAQ:GLMD). Mr. Blacher also held senior positions in licensing and investing at Teva Pharmaceuticals, portfolio management at Deutsche Asset Management and equity research at Morgan Stanley, as well as in Mergers & Acquisitions at Lehman Brothers. Mr. Blacher holds an MBA in Finance from Columbia Business School.

***Jeff Charpentier, Chief Financial Officer***

Mr. Charpentier is a veteran of the biopharmaceutical industry with 26 years of experience. Mr. Charpentier has held a series of senior financial roles at several public and private companies in the pharmaceutical and technology sectors where he led multiple equity financings, raising in excess of \$150M and concluded a number of corporate partnering/product sale transactions. Mr. Charpentier also currently serves as CFO for ImStar Therapeutics Inc. and Proactive Immune Sciences Corporation. Mr. Charpentier previously served as CFO for Lifebank Corp. (through to successful company sale in 2012), Inex Pharmaceuticals Corporation (now Arbutus Biopharma Corp.), and Chromos Molecular Systems Inc. Mr. Charpentier has a Bachelor of Commerce degree from the University of British Columbia and is a member of the Chartered Professional Accountants of BC.

***Sazzad Hossain, PhD, Chief Scientific Officer***

Dr. Hossain has more than 20 years of academic and industrial experience in new drug discovery, natural health product development. He was Group Leader and Senior Scientist at Biotechnology Research Institute of National Research Council Canada, Government of Canada's prime biotechnology research organization where he set up pharmacology laboratory to evaluate safety and efficacy of new drugs under development in the areas of cancer, cardiovascular and ocular diseases. Prior to joining the National Research Council Canada, he was at Xenon Pharmaceuticals in Vancouver, B.C, where was Associate Director of Pharmacology and led pharmacology teams targeting pain, inflammation and cardiovascular diseases. Dr. Hossain received his PhD in Biology from Moscow State Academy of Veterinary Medicine & Biotechnology and received post-doctoral training in the Department of

Nutritional Science and Department of Medical Genetics of University of British Columbia. He was associate professor of pharmacology at Federal University of Minas Gerais, Brazil between 1988 -1996. He is the author of more than 40 peer-reviewed papers, primarily in the pharmacology, genetics and nutritional sciences.

***Eric Hsu, PhD, Vice President of Preclinical Research and Development***

Dr. Hsu has over 18 years of scientific leadership experience in the field of gene therapy. Prior to joining InMed, he held various positions within enGene Inc., including V.P. of Research and V.P. of Scientific Affairs and Operations. His experience includes a wide array of activities, including benchtop research, formulation development and manufacturing process development, as well as patent prosecution, vendor contract negotiations and execution, and research partnerships. Dr. Hsu is considered to be an expert in gene transfer and gene expression using vector systems. He received his Doctorate from the Department of Medical Biophysics at University of Toronto and his Bachelor's degree from McGill University.

***Alexandra D.J. Mancini, SVP – Clinical and Regulatory Affairs***

Ms. Mancini has over 30 years of global biopharmaceutical R&D experience with a particular emphasis on clinical development and regulatory affairs. Ms. Mancini has been an executive with several biotech companies, overseeing a wide range of drug development activities. As Sr. VP of Clinical & Regulatory Affairs at Sirius Genomics, her role included identifying and managing external resources for medical expertise in sepsis; clinical data management; and statistical theory, programming and analyses. While at Inex Pharmaceuticals as Sr. VP of Clinical & Regulatory Affairs, Ms. Mancini oversaw Clinical Research, Medical Affairs, Clinical Data Management, Medical Writing, Regulatory Affairs, and Quality Assurance for oncology. She served as VP of Regulatory Affairs at QLT Inc. for oncology and ocular diseases, playing a significant role in the development of VISUDYNE<sup>®</sup> from the preclinical stage through to its approval as the first drug for age-related macular degeneration. While at QLT, Ms. Mancini also led the regulatory approval process for the anticancer drug PHOTOFRIN<sup>®</sup> and its associated medical devices, the first drug-device combination product approved by the FDA. Ms. Mancini has led the data analysis and assimilation, writing, submission and subsequent defense of drug submissions to regulatory agencies around the world, leading to several drug approvals and label extensions. Ms. Mancini holds a Master of Science degree from the University of Toronto. She is also a Visiting Lecturer at the Segal Graduate School of Business, Simon Fraser University.

**Security Holdings of the Directors and Officers**

As at the date of this AIF, as a group, the directors and executive officers of InMed beneficially own, or exercise control or direction over, directly or indirectly, a total of 3,612,725 Common Shares, representing approximately 2.1% of the currently issued and outstanding Common Shares (excluding the Common Shares issuable upon the exercise of the aggregate of 15,870,000 options and 272,225 warrants held by the directors and executive officers of InMed).

**Cease Trade Orders, Bankruptcies, Penalties and Sanctions**

As at the date of this AIF:

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

- (i) was subject to an order (as defined below) that was issued while the director or executive officer was acting in the capacity as director, chief executive officer or chief financial officer; or
- (ii) was subject to an order that was issued after the director or executive officer ceased to be a director, chief executive officer or chief financial officer and which resulted from an event that occurred while that person was acting in the capacity as director, chief executive officer or chief financial officer.

(b) No director or executive officer of InMed, and to the best of the knowledge of InMed, no shareholder holding a sufficient number of InMed's securities to affect materially the control of InMed:

- (i) is, as at the date of this AIF, or has been within 10 years before the date of this AIF, a director or executive officer of any company (including InMed) that, while that person was acting in that capacity, or within a year of that person ceasing to act in that 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 the assets of the director, executive officer or shareholder.
- (c) No director or executive officer of InMed, and to the best of the knowledge of InMed, no shareholder holding a sufficient number of InMed's securities to affect materially the control of InMed, has been subject to:
- (i) any penalties or sanctions imposed by a court relating to securities legislation or by a securities regulatory authority or has entered into a settlement agreement with a securities regulatory authority; or
  - (ii) 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 with respect to InMed.

For the purposes of (a) above, “**order**” means:

- (a) a cease trade order;
- (b) an order similar to a cease trade order; or
- (c) 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.

### **Conflicts of Interest**

There are currently no existing or potential material conflicts of interests between InMed and any of its directors and officers other than those otherwise set out herein.

## **AUDIT COMMITTEE INFORMATION**

### **Charter of the Audit Committee**

The full text of the current Terms of Reference for the Audit Committee is attached as Schedule A to this AIF.

### **Composition of the Audit Committee**

The current members of the audit committee are Andrew Hull, Martin Bott and Adam Cutler (Chairman). All members of the audit committee are “financially literate”, as such term is defined in NI 52-110 – Audit Committees, or NI 52-110. All members of the committee are considered “independent” under NI 52-110.

### **Relevant Education and Experience**

See the respective biographies of each member of the Audit Committee in “*Directors and Management - Profile of the Directors and Management*” for a description of the experience that is relevant to the performance of their responsibilities as Audit Committee members.

### Reliance on Certain Exemptions

At no time since the commencement of InMed’s most recently completed financial year has the Company relied on any of the exemptions provided in NI 52-110.

### Audit Committee Oversight

At no time since the commencement of the Company’s most recently completed financial year have any recommendations by the Audit Committee respecting the appointment and/or compensation of the Company’s external auditors not been adopted by the board of directors of InMed.

### Pre-Approval Policies and Procedures

The policy and procedures relating to the pre-approval of non-audit services provided to the Company are described in the Terms of Reference for the Audit Committee attached as Schedule A to this AIF.

### External Auditor Service Fees

The aggregate fees billed by InMed’s external auditors in each of the last two fiscal years for audit fees are as follows:

Fee category	Year Ended June 30, 2018	Year Ended June 30, 2017
Audit Fees	\$24,500	\$24,500
Audit-Related Fees	\$24,000	\$5,250
Tax Fees	\$4,200	\$3,000
All Other Fees	\$31,500	\$Nil
<b>Total</b>	<b>\$84,200</b>	<b>\$32,750</b>

“**Audit Fees**” are the aggregate fees billed by the Company’s external auditor for services provided for the audit of InMed’s annual financial statements.

“**Audit-Related Fees**” are the aggregate fees billed for assurance and related services by the Company’s external auditor that are reasonably related to the performance of the audit or review of the Company’s financial statements.

“**Tax Fees**” are the aggregate fees billed by InMed’s external auditor for tax compliance, tax advice and tax planning services.

“**All Other Fees**” are the aggregate fees billed by InMed’s external auditor for products and services not included in the other categories of fees described above such as work associated with the filing of prospectuses by the Company.

### LEGAL PROCEEDINGS AND REGULATORY ACTIONS

InMed was not involved in any legal proceedings during the year ended June 30, 2018 that had, or could have, a material adverse effect on InMed. Moreover, to the knowledge of InMed’s management, InMed is not currently involved in any outstanding, threatened or pending litigation that could have a material adverse effect on InMed.

To the knowledge of InMed, during the financial year ended June 30, 2018, there were no: (i) penalties or sanctions imposed against InMed by a court relating to securities legislation or by a securities regulatory authority; (ii) any other penalties or sanctions imposed by a court or regulatory body against InMed that would likely be considered important to a reasonable investor in making an investment decision; or (iii) settlement agreements InMed entered into before a court relating to securities legislation or with a securities regulatory authority.

### **INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS**

Except as described elsewhere in this AIF, there have been no related party transactions in the three most recently completed financial years of InMed that required disclosure under any applicable Canadian securities laws other than disclosed in note 13 to Company's 2018 audited consolidated financial statements, note 15 to the Company's 2017 audited financial statements and note 13 to the Company's 2016 audited consolidated financial statements, copies of which audited consolidated financial statements are available on SEDAR at [www.sedar.com](http://www.sedar.com).

### **TRANSFER AGENT AND REGISTRAR**

The transfer agent and registrar for the Common Shares is Computershare Investor Services Inc. at its principal offices located in Vancouver, British Columbia and Toronto, Ontario.

The transfer agent and registrar for InMed's outstanding May 2017 Warrants and June 2018 Warrants is, pursuant to the respective warrant indentures, Computershare Trust Company of Canada at its principal offices in Vancouver, British Columbia.

### **MATERIAL CONTRACTS**

The following are material contracts of InMed required to be filed on SEDAR pursuant to NI 51-102:

1. The share purchase agreement with Biogen Sciences Inc. dated May 10, 2014, as more particularly described above under "*General Development of the Business – Three Year History*", a copy of which is available on SEDAR at [www.sedar.com](http://www.sedar.com).
2. The purchase agreement with Dr. Sazzad Hossain dated October 28, 2015, as more particularly described above under "*General Development of the Business – Three Year History*", a copy of which is available on SEDAR at [www.sedar.com](http://www.sedar.com).
3. The warrant indenture with Computershare dated May 31, 2017, as more particularly described above under "*Capital Structure – Share Purchase Warrants*", a copy of which is available on SEDAR at [www.sedar.com](http://www.sedar.com).
4. The warrant indenture with Computershare dated June 21, 2018, as more particularly described above under "*Capital Structure – Share Purchase Warrants*", a copy of which is available on SEDAR at [www.sedar.com](http://www.sedar.com).

### **INTERESTS OF EXPERTS**

KPMG LLP are the auditors of the Company and have confirmed that they are independent with respect to the Company within the meaning of the relevant rules and related interpretations prescribed by the relevant professional bodies in Canada and any applicable legislation or regulation.

### **ADDITIONAL INFORMATION**

Additional information relating to InMed may be found on SEDAR at [www.sedar.com](http://www.sedar.com). Additional information, including directors' and officers' remuneration and indebtedness, principal holders of InMed's securities, and securities authorized for issuance under equity compensation plans, if applicable, is contained in InMed's information circular dated November 1, 2017 a copy of which has been filed on SEDAR and is available at [www.sedar.com](http://www.sedar.com). Additional financial information is provided in InMed's audited consolidated financial statements and management's discussion and analysis for InMed's most recently completed financial year, copies of which have been filed on SEDAR and are available at [www.sedar.com](http://www.sedar.com).

## SCHEDULE A



### INMED PHARMACEUTICALS INC.

#### TERMS OF REFERENCE FOR THE AUDIT COMMITTEE

##### PURPOSE

InMed Pharmaceuticals Inc. (the “**Company**”) shall appoint an audit committee (the “**Committee**”) to assist the board of directors (the “**Board**”) of the Company in fulfilling its responsibilities of oversight and supervision of the accounting and financial reporting practices and procedures on behalf of the Company and its direct and indirect subsidiaries, the adequacy of internal accounting controls and procedures, and the quality and integrity of the financial statements of the Company. In addition, the Committee is responsible for directing the auditors’ examination of specific areas, for the selection of the independent auditors of the Company and for the approval of all non-audit services for which the auditors of the Company may be engaged.

##### I. STRUCTURE AND OPERATIONS

The Committee shall be comprised of at least three members, each of whom shall be a director of the Company and shall be “independent” within the meaning of National Instrument 52-110 – *Audit Committees* (“**NI 52-110**”).

Each member of the Committee shall satisfy the “financial literacy” requirement of NI 52-110, by having the ability to read and understand a set of financial statements that present a breadth and level of complexity of accounting issues that can reasonably be expected to be raised by the financial statements of the Company.

The members of the Committee shall be annually appointed by the Board and shall serve until such member’s successor is duly elected and qualified or until such member’s earlier resignation or removal. The members of the Committee may be removed, with or without cause, by a majority of the Board.

##### II. CHAIR OF THE COMMITTEE

Unless the Board elects a Chair of the Committee, the members of the Committee shall designate a Chair by the majority vote of the full Committee membership.

The Chair of the Committee shall:

- (d) Call and conduct the meetings of the Committee;
- (e) Be entitled to vote to resolve any ties;
- (f) Prepare and forward to members of the Committee the agenda for each meeting of the Committee, and include, in the agenda, any items proposed for inclusion in the agenda by any member of the Committee;
- (g) Review with the Chief Financial Officer (“**CFO**”) and the auditors for the Company any matters referred to the Chair by the CFO or the auditors of the Company;

- (h) Appoint a secretary, who need not be a member of the Committee, to take minutes of the meetings of the Committee; and
- (i) Act in a manner that the Committee meetings are conducted in an efficient, effective and focused manner.

### **III. MEETINGS**

The Committee shall meet at least quarterly or more frequently as circumstances dictate. As part of its goal to foster open communication, the Committee shall periodically meet with management and the external auditors in separate sessions to discuss any matters that the Committee or each of these groups believes should be discussed privately. The Committee may meet privately with outside counsel of its choosing and the CFO of the Company, as necessary. In addition, the Committee shall meet with the external auditors and management quarterly to review the Company's financial statements in a manner consistent with that outlined in these Terms.

The Committee may invite to its meetings any partners of the Company, management and such other persons as it deems appropriate in order to carry out its responsibilities. The Committee may exclude from its meetings any persons it deems appropriate in order to carry out its responsibilities.

A majority of the Committee members, but not less than two, shall constitute a quorum. A majority of members present at any meeting at which a quorum is present may act on behalf of the Committee. The Committee may meet by telephone or videoconference and may take action by unanimous written consent with respect to matters that may be acted upon without a formal meeting.

The Committee shall maintain minutes or other records of meetings and activities of the Committee.

Notice of the time and place of every meeting shall be given in writing or electronic communication to each member of the Committee at least 24 hours prior to the time fixed for such meeting provided however, that a member may in any manner waive a notice of a meeting. Attendance of a member at a meeting is a waiver of notice of the meeting, except where a member attends a meeting for the express purpose of objecting to the transaction of any business on the grounds that the meeting is not lawfully called.

### **IV. RESPONSIBILITIES, DUTIES AND AUTHORITY**

The following functions shall be the common recurring activities of the Committee in carrying out its responsibilities outlined in these Terms. These functions should serve as a guide with the understanding that the Committee may carry out additional functions and adopt additional policies and procedures as may be appropriate in light of changing business, legislative, regulatory, legal and other conditions. The Committee shall also carry out any other responsibilities and duties delegated to it by the Board from time to time related to the purposes of this Committee.

The Committee in discharging its oversight role is empowered to investigate any matter of interest or concern that the Committee deems appropriate. In this regard, the Committee shall have the authority to retain outside counsel, accounting or other advisors for this purpose, including authority to approve the fees payable to such advisors and other terms of retention. In addition, the Committee shall have the authority to communicate directly with both external and internal auditors of the Company.

The Committee shall be given full access to the Board, management, employees and others, directly and indirectly responsible for financial reporting, and independent accountants, as necessary, to carry out these responsibilities. While acting within the scope of this stated purpose, the Committee shall have all the authority of the Board.

The Committee shall be responsible for assessing the range of financial and other risks to the business and affairs of the Company that the Board shall focus on, and make recommendations to the Board about how appropriate responsibilities for continuing to identify, monitor and manage these risks are to be delegated. The Committee shall review and discuss with management and the internal and external auditors all major financial risk exposures and the steps management has taken to monitor/control those exposures. In addition, the Committee shall encourage

continuous improvement of, and foster adherence to, the Company's financial policies, procedures and practices at all levels in the organization; and provide an avenue of communication among the independent auditors, management and the Board.

Absent actual knowledge to the contrary (which shall promptly reported to the Board), each member of the Committee shall be entitled to rely on: (i) the integrity of those persons or organizations within and outside the Company from which it receives information; (ii) the accuracy of the financial and other information provided to the Committee by such persons or organizations; and (iii) representations made by management and the external auditors, as to any information technology, internal audit and other non-audit services provided by the external auditors to the Company and its subsidiaries.

## **V. SPECIFIC RESPONSIBILITIES AND ACTIVITIES**

### **A. Document Reports/Reviews**

2. *Annual Financial Statements.* The Committee shall review with management and the external auditors, both together and separately, prior to public dissemination:

- (a) the annual audited consolidated financial statements;
- (b) the external auditor's review of the annual consolidated financial statements and their report;
- (c) any significant changes that were required in the external audit plan;
- (d) any significant issues raised with management during the course of the audit, including any restrictions on the scope of activities or access to information; and
- (e) those matters related to the conduct of the audit that are required to be discussed under generally accepted auditing standards applicable to the Company.

Following completion of the matters contemplated above, the Committee shall make a recommendation to the Board with respect to the approval of the annual financial statements with such changes contemplated and further recommended, as the Committee considers necessary.

3. *Interim Financial Statements.* The Committee shall review with management and may review with the external auditors, both together and separately, prior to public dissemination, the interim unaudited consolidated financial statements of the Company, including to the extent the Committee considers appropriate, a discussion with the external auditors of those matters required to be discussed under generally accepted auditing standards applicable to the Company.

4. *Management's Discussion and Analysis.* The Committee shall review with management and the external auditors, both together and separately prior to public dissemination, the annual Management's Discussion and Analysis of Financial Condition and Results of Operations ("**MD&A**") and the Committee shall review with management and may review with the external auditors, interim MD&A.

5. *Approval of Annual MD&A, Interim Financial Statements and Interim MD&A.* The Committee shall make a recommendation to the Board with respect to the approval of the annual MD&A with such changes contemplated and further recommended by the Committee as the Committee considers necessary. In addition, the Committee shall approve the interim financial statements and interim MD&A of the Company, if the Board has delegated such function to the Committee. If the Committee has not been delegated this function, the Committee shall make a recommendation to the Board with respect to the approval of the interim financial statements and interim MD&A with such changes contemplated and further recommended as the Committee considers necessary.

6. *Press Releases.* With respect to press releases by the Company:
    - (a) The Committee shall review the Company’s financial statements, MD&A and annual and interim earnings press releases before the Company publicly discloses this information.
    - (b) The Committee shall review with management, prior to public dissemination, the annual and interim earnings press releases (paying particular attention to the use of any “pro forma” or “adjusted non-IFRS” information) as well as any financial information and earnings guidance provided to analysts and rating agencies.
    - (c) The Committee shall be satisfied that adequate procedures are in place for the review of the Company’s public disclosure of financial information extracted or derived from the Company’s financial statements, other than public disclosure referred to in Section V.A.4 of these Terms, and periodically assess the adequacy of those procedures.
  7. *Reports and Regulatory Returns.* The Committee shall review and discuss with management, and the external auditors to the extent the Committee deems appropriate, such reports and regulatory returns of the Company as may be specified by law.
  8. *Other Financial Information.* The Committee shall review the financial information included in any prospectus, annual information form or information circular with management and, at the discretion of the Committee, the external auditors, both together and separately, prior to public dissemination, and shall make a recommendation to the Board with respect to the approval of such prospectus, annual information form or information circular with such changes contemplated and further recommended as the Committee considers necessary.
- B. Financial Reporting Processes**
9. *Establishment and Assessment of Procedures.* The Committee shall satisfy itself that adequate procedures are in place for the review of the public disclosure of financial information extracted or derived from the financial statements of the Company and assess the adequacy of these procedures annually.
  10. *Application of Accounting Principles.* The Committee shall assure itself that the external auditors are satisfied that the accounting estimates and judgements made by management, and their selection of accounting principles reflect an appropriate application of such accounting principles.
  11. *Practices and Policies.* The Committee shall review with management and the external auditors, together and separately, the principal accounting practices and policies of the Company.
- C. External Auditors**
12. *Oversight and Responsibility.* In respect of the external auditors of the Company:
    - (a) The Committee shall recommend to the Board the external auditors nominated for the purpose of preparing or issuing an auditor’s report or performing other audit, review or attest services for the Company and the compensation of the external auditors.
    - (b) The Committee is directly responsible for overseeing the work of the external auditors engaged for the purpose of preparing or issuing an auditor’s report or performing other audit, review or attest services for the Company, including the resolution of disagreements between management and the external auditors regarding financial reporting.
  13. *Reporting.* The external auditors shall report directly to the Committee and are ultimately accountable to the Committee.

14. *Performance and Review.* The Committee shall annually review the performance of the external auditors and recommend to the Board the appointment of the external auditors or approve any discharge of the external auditors when circumstances warrant, for the purpose of preparing or issuing an auditor's report or performing other audit, review or attest services for the Company.
15. *Annual Audit Plan.* The Committee shall review with the external auditors and management, together and separately, the overall scope of the annual audit plan and the resources the external auditors will devote to the audit. The Committee shall annually review and approve the fees to be paid to the external auditors with respect to the annual audit.
16. *Non-Audit Services.*
- (a) "Non-audit services" means all services performed by the external auditors other than audit services. The Committee shall pre-approve all non-audit services to be provided to the Company or its subsidiaries by the Company's external auditor and permit all non-audit services, other than non-audit services where:
    - (i) the aggregate amount of all such non-audit services that were not pre-approved is reasonably expected to constitute no more than five per cent of the total amount of fees paid by the Company and its subsidiaries to the Company's external auditor during the fiscal year in which the services are provided;
    - (ii) the Company or its subsidiary, as the case may be, did not recognize the services as non-audit services at the time of the engagement; and
    - (iii) the services are promptly brought to the attention of the Committee and approved, prior to the completion of the audit, by the Committee or by one or more of its members to whom authority to grant such approvals had been delegated by the Committee.
  - (b) The Committee may delegate to one or more members of the Committee the authority to grant such pre-approvals for non-audited services. The decisions of such member(s) regarding approval of "non-audit" services shall be reported by such member(s) to the full Committee at its first scheduled meeting following such pre-approval.
  - (c) The Committee shall adopt specific policies and procedures for the engagement of the non-audit services if:
    - (i) the pre-approval policies and procedures are detailed as to the particular services;
    - (ii) the Committee is informed of each non-audit service; and
    - (iii) the procedures do not include delegation of the Committee's responsibilities to management.
17. *Independence Review.* The Committee shall review and assess the qualifications, performance and independence of the external auditors, including the requirements relating to such independence of the law governing the Company. At least annually, the Committee shall receive from and review with the external auditors, their written statement delineating all relationships with the Company and, if necessary, recommend that the Board takes appropriate action to satisfy themselves of the external auditors' independence and accountability to the Committee.

**D. Reports to Board**

18. *Reports.* In addition to such specific reports contemplated elsewhere in these Terms, the Committee shall report regularly to the Board regarding such matters, including:

- (a) with respect to any issues that arise with respect to the quality or integrity of the financial statements of the Company, compliance with legal or regulatory requirements by the Company, or the performance and independence of the external auditors of the Company;
  - (b) following meetings of the Committee; and
  - (c) with respect to such other matters as are relevant to the Committee's discharge of its responsibilities.
19. *Recommendations.* In addition to such specific recommendations contemplated elsewhere in these Terms, the Committee shall provide such recommendations as the Committee may deem appropriate. The report to the Board may take the form of an oral report by the Chair or any other member of the Committee designated by the Committee to make such report.

**E. Whistle Blowing**

20. *Procedures.* The Committee shall establish procedures for:
- (a) the receipt, retention and treatment of complaints received by the Company regarding questionable accounting, internal accounting controls, or auditing matters; and
  - (b) the confidential, anonymous submission by employees and of concerns regarding questionable accounting or auditing matters.
21. *Notice to Employees.*
- (a) To comply with the above, the Committee shall ensure each of the Company and its subsidiaries advises all employees, by way of a written code of business conduct and ethics (the “Code”), or if such Code has not yet been adopted by the respective board, by way of a written or electronic notice, that any employee who reasonably believes that questionable accounting, internal accounting controls, or auditing matters have been employed by the Company or their external auditors is strongly encouraged to report such concerns by way of communication directly to the Chair. Matters referred may be done so anonymously and in confidence.
  - (b) None of the Company or its subsidiaries shall take or allow any reprisal against any employee for, in good faith, reporting questionable accounting, internal accounting, or auditing matters. Any such reprisal shall itself be considered a very serious breach of this policy.
  - (c) All reported violations shall be investigated by the Committee following rules of procedure and process as shall be recommended by outside counsel.

**F. General**

22. *Access to Counsel.* The Committee shall review, periodically, with outside counsel of its choosing, any legal matter that could have a significant impact on the financial statements, the Company's compliance policies and any material reports or inquiries received from regulators or governmental agencies.
23. *Hiring of Partners and Employees of External Auditors.* The Committee shall annually review and approve the Company's hiring policies regarding partners, employees and former partners and employees of the present and former external auditors of the Company.
24. *Forward Agenda.* The Committee may annually develop a calendar of activities or forward agenda to be undertaken by the Committee for each ensuing year and to submit the calendar/agenda in the appropriate format to the Board of Directors following each annual general meeting of shareholders.

25. *General.* The Committee shall perform such other duties and exercise such powers as may, from time to time, be assigned or vested in the Committee by the Board, and such other functions as may be required of an audit committee by law, regulations or applicable stock exchange rules.

#### **VI. ANNUAL PERFORMANCE REVIEW EVALUATION**

26. The Committee shall perform a review and evaluation, annually, of the performance of the Committee and its members, including a review of the compliance of the Committee with these Terms. In addition, the Committee shall evaluate, annually, the adequacy of these Terms and recommend any proposed changes to the Board.
27. The Committee shall annually review transactions involving directors and officers, including a review of travel expenses and entertainment expenses, related party transactions and any conflicts of interests.
28. Management shall be required to provide the Committee, at least annually, a report on internal controls, including reasonable assurance that such controls are adequate to facilitate reliable and timely financial information. The Committee shall also review and follow-up on any areas of internal control weakness identified by the external auditors with the auditors and management.
29. The Committee shall discuss with management its process for performing its required quarterly certifications under National Instrument 52-109 – *Certification of Disclosure in Issuers' Annual and Interim Filings*, including the evaluation of the effectiveness of disclosure controls by the Chief Executive Officer and CFO of the Company.

**These Terms were approved by the Board on September 12, 2018.**