

QUARTERLY NEWSLETTER

A clinical stage pharmaceutical company focused on the research and development of light activated Photo Dynamic Compounds (“PDC”) and their associated drug formulations used to safely and effectively destroy various cancers, bacteria and viruses.



OVERVIEW:

The Company’s main focus continue to be the completion of:

1. Phase II Non-Muscle Invasive Bladder Cancer (“NMIBC”) clinical study for BCG- unresponsive Carcinoma In-Situ (“CIS”) (“Study II”) patients.
2. Glio Blastoma Multiforme (“GBM”) and Non-Small Cell Lung Cancer (“NSCLC”) toxicology studies to allow submission of a Phase Ib clinical study for both indications to regulatory authorities for approval.
3. Coronavirus (BSL-3) vaccine research and development.

COVID-19 Pandemic Update

Due to the continued uncertainty associated with the COVID-19 pandemic, the impact on the Company’s business, operations and financial performance cannot be fully quantified at this time. Theralase continues to closely monitor the situation, in conjunction with municipal, provincial, and federal guidelines, in order to best manage its business in compliance with health and safety best practices.

Financial Statements

Theralase® continues to experience reduced sales due to the ongoing COVID-19 pandemic and has taken actions to reduce expenses; specifically, terminating the positions of non essential personnel and instituting a temporary hiring freeze on full-time employees. The hiring freeze will be lifted, subject to the Canadian and United States economies demonstrating recovery from the COVID-19 pandemic.

[Q3 2020 Financial Statement](#)

Update on Study II

Theralase® has 5 Canadian clinical study sites open for patient enrollment and treatment Study II; specifically:

Study Site	Location
University Health Network (“UHN”)	Toronto, Ontario
London Health Sciences Centre (“LHSC”)	London, Ontario
Nova Scotia Health Authority (“NSHA”)	Halifax, Nova Scotia
University of British Columbia (“UBC”)	Vancouver, British Columbia
McGill University Health Centre (“MUHC”)	Montreal, Quebec

Theralase has received study level approval through a central Institutional Review Board (“IRB”) to launch Study II in 6 US Clinical Sites subject to site level IRB approval. To date the following US clinical sites have received site level IRB approval to commence patient enrollment and treatment:

Study Site	Location
Virginia Urology (“VU”)	Richmond, Virginia
Urology Associates P.C. (“UA”)	Nashville, Tennessee
MidLantic Urology (“MU”)	Bala Cynwyd, Pennsylvania
Carolina Urologic Research Centre (“CURC”)	Myrtle Beach, SC



The 2 remaining US clinical study sites are expected to receive site level IRB approval in 1Q2021. Theralase is focused on its target of enrolling and treating 11 additional patients in early 2021 for a total of 25 patients for potential Breakthrough Designation (“BTD”) approval and approximately 100 patients in 2021 / 2022 to complete Study II.

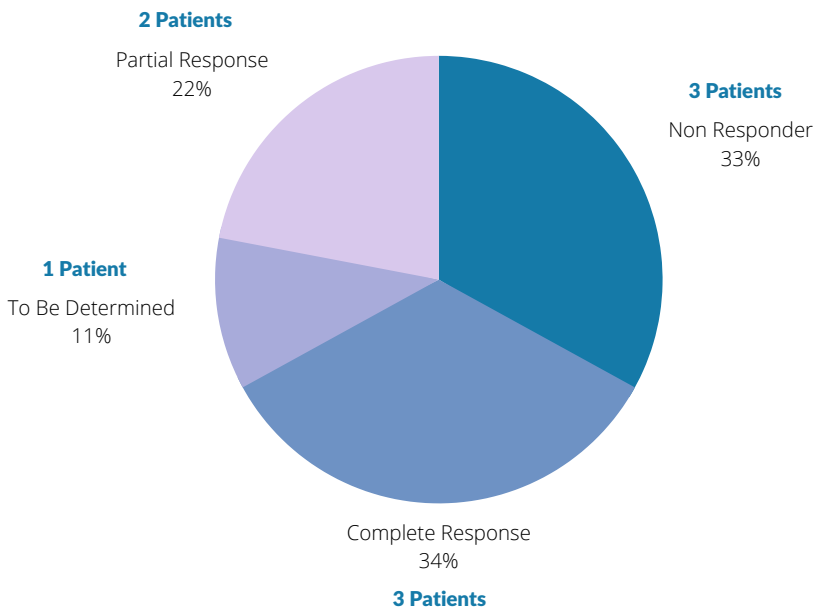
Patient enrollment and treatment rates have been significantly delayed due to the COVID-19 pandemic restrictions but, are expected to improve once Canada and the US recover from the COVID-19 pandemic. Canadian study sites placed themselves on temporary hold commencing March 20, 2020 and resumed normal operations between August 12, 2020 and September 24, 2020. Although Canadian clinical study sites recruiting activities were re-commenced in Q4 2020; patient recruitment and treatment activities have been limited due to the second wave of COVID-19. With the addition of 4 additional US based clinical study sites in January 2021, Theralase is hopeful that patient recruitment and treatment activities will increase in 1Q2021 and throughout 2021 to help achieve the Company’s strategic objectives.

Study II Interim Results

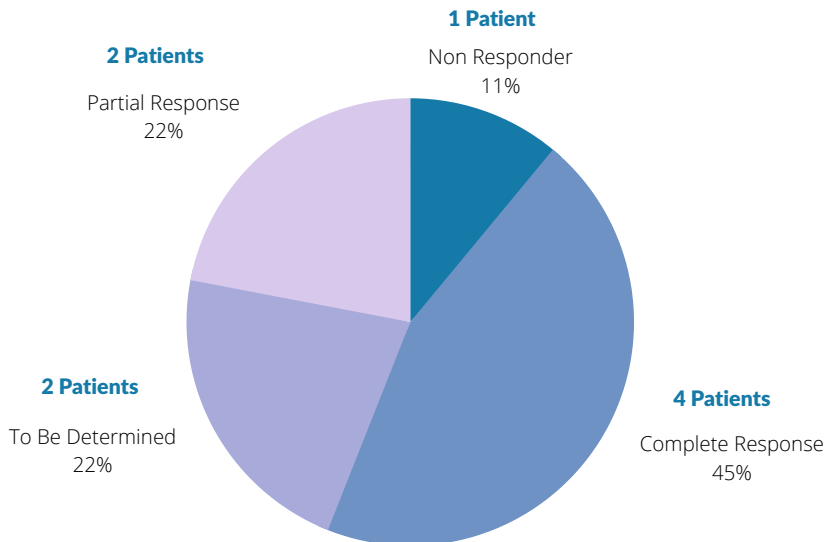
Patients Treated	
Primary Study Treatment	14
Maintenance Study Treatment	5
Removed from Study	5
Remaining Patients in Study	9

The results of the remaining 9 patients at the 90 day and 180 day assessment is as follows:

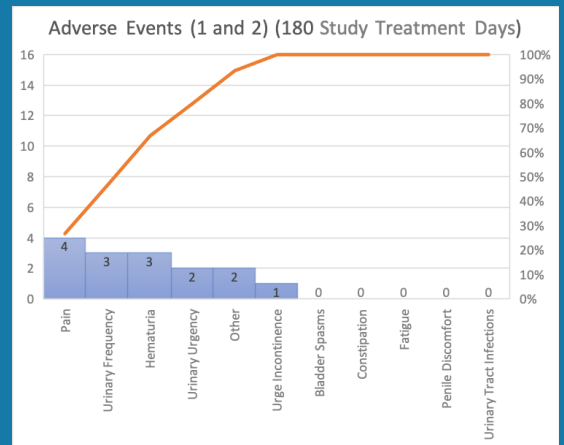
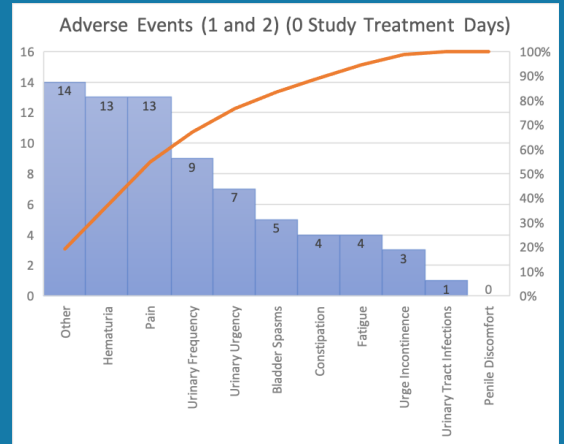
90 DAY ASSESSMENT



180 DAY ASSESSMENT



Adverse Events ("AEs")



Study II commenced in April 2019 with an estimated completion time of approximately 3 to 4 years and an estimated cost of approximately \$9 to \$11 million. The timing and cost may vary significantly depending on numerous factors including: number of clinical study sites enrolling and treating patients, clinical study site patient enrollment rates, patient compliance, successful achievement of Study II primary, secondary and tertiary endpoints and the ability of participating clinical study sites to enroll and treat patients considering challenges caused by current COVID-19 pandemic restrictions.

GBM & NSCLC Toxicology Studies

Theralase® has steered the research and development of these Photo Dynamic Compounds (“PDCs”) through scientific and preclinical research to fine-tune the photophysical and photochemical properties of the PDCs, by the inventor, while demonstrating Type I (oxygen independent) and II (oxygen dependent) photoreactions and activation in hypoxia. By combining these PDCs with transferrin (human glycoprotein), as a delivery system it has been pre-clinically demonstrated that transferrin is able to significantly increase the resistance of TLD-1433, the lead drug candidate, to photobleaching (loss of potency of the PDC over time), Reactive Oxygen Species (“ROS”) production (ability to destroy cancer cells quickly and effectively), select tumour uptake (destruction of cancer cells, while sparing healthy cells), anti-cancer efficacy (efficiency in cancer cell destruction) and decreasing systemic toxicity (damage to healthy cells and/or organs) of the PDC. This makes Rutherrin® (TLD-1433 + transferrin) attractive for systemic treatment of recurrent, deep seated and/or progressive cancers.

The Company continues to conduct extensive scientific and preclinical research towards new oncology indications and has developed significant expertise and intellectual property assets regarding its patented PDCs, in pursuit of this goal.

Rutherrin®, a systemic formulation of TLD-1433 suitable for intravenous (“IV”) injection is being investigated to be injected via IV into the body, with a mandate of “hunting” and “destroying” cancer cells; wherever, they may reside in the body. The Company has demonstrated a significant anti-cancer efficacy of Rutherrin®, when activated by laser light or radiation treatment across, numerous preclinical in-vitro (cell lines) and in-vivo (animal) models focused on GBM and NSCLC.

The Company has commenced non Good Laboratory Practice (“GLP”) toxicology studies with Rutherrin® to determine the Maximum Tolerated Dose (“MTD”) of Rutherrin® to be translated to the recommended human dose, when administered systemically into the human body, via IV. Theralase® has completed one animal model and is working to complete the second animal model. If successful, Theralase® plans to commence a GLP toxicology studies with an aim to commencing a Phase Ib clinical study in GBM and NSCLC in 2022.

Due to the limitations of using laser light to activate Rutherrin® in deep oncological targets, Theralase’s research strongly suggests that Rutherrin® may be activated with radiation therapy, which is able to increase the ‘tumour’s damage zone’ and the effectiveness of Theralase’s Anti-Cancer Therapy (“ACT”) beyond the reach of light in the body.



Dr. Michael Jewett named to the Order of Canada

Michael A. S. Jewett, Chairman, Medical Scientific and Advisory Board of Theralase®, was appointed to the Order of Canada for his life-saving innovations in surgical oncology and for his advocacy of patient-centred clinical care. He is an award winning and internationally-recognized uro-oncologist, known for his contributions in the fields of kidney, testicular and bladder cancer. He served as the Chairman of the Division of Urology at the University of Toronto and Head of Urology at University Health Network / Princess Margaret Cancer Center from 1991 to 2002 and remains an active clinician and investigator at UHN.

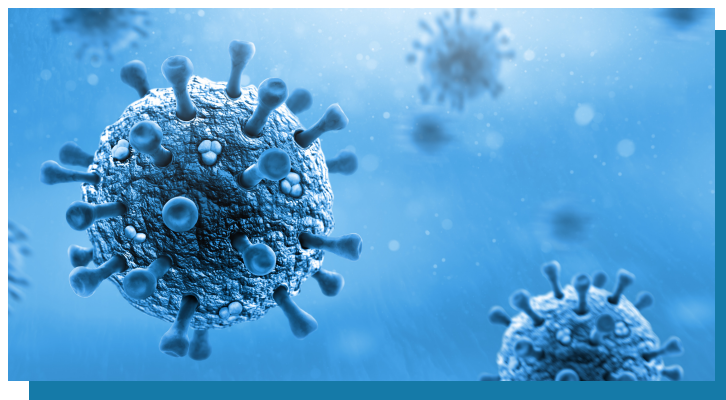
The Order of Canada is one of our country’s highest civilian honours. Created in 1967, the Order of Canada recognizes outstanding achievement, dedication to the community and service to the nation. More than 7,000 people from all sectors of society have been invested into the Order. Those who bear the Order’s iconic snowflake insignia have changed our nation’s measure of success and, through the sum of their accomplishments, have helped us build a better Canada.

Coronavirus (BSL-3) Vaccine Research

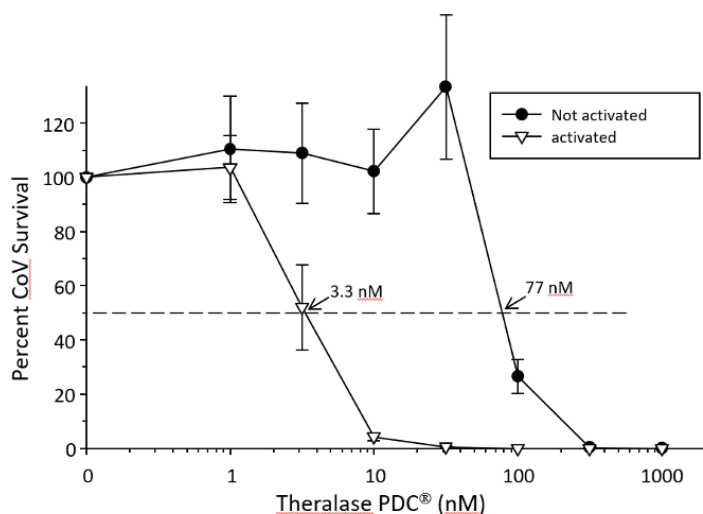
Theralase® executed a Sponsored Research Agreement (“SRA”) with the University of Manitoba (“UM”) Medical Microbiology department in 3Q2020 to commence development of a coronavirus vaccine utilizing Theralase’s patented and proprietary PDCs. The primary objective of the SRA was to investigate the efficacy of Theralase’s lead PDC to destroy a variety of viruses; including: H1N1 Influenza, Zika and coronaviruses (Biological Safety Level (“BSL”) 2). The secondary objective was to optimize the concentration of PDC required, the activation methodology and how to potentially administer the treatment to humans to be used as a vaccine (prevention of a patient from contracting COVID-19) (BSL-3).

Theralase® previously reported that the Company’s PDC technology was effective in the destruction of Influenza and Zika viruses at low nanomolar concentrations. These studies were expanded to include coronavirus (BSL-2). As a cautionary note, COVID-19 is caused by coronavirus (BSL-3), not coronavirus (BSL-2). A rapid test was established to measure coronavirus destruction and using this new assay the Theralase® PDC technology was able to destroy coronavirus (BSL-2) with drug doses 5 times lower than what was used to kill Influenza H1N1 virus and Zika virus. These drug doses are significantly lower than those used by the Company to treat cancers and are considered safe for human use. All coronaviruses are highly similar in their structure and these new results strongly suggest that Theralase’s proposed vaccine could be highly effective against the SARS-CoV-2 virus responsible for COVID-19.

Further studies have shown that the human coronavirus (CoV) appears to be much more sensitive to the action of the activated Theralase PDC vaccine, with as low a dose of 3.3nM required to inactivate 50%; whereas; 9.2nM was required to inactivate the same amount of Influenza and 12nM was required inactivate the same amount of Zika Virus. Similarly, the amount of PDC required to inactivate 99.9% of each virus are 61nM for CoV, 322nM for Zika Virus and 497nM for Influenza. Thus, the Theralase PDC is 3 to 5 times more effective against CoV compared to the other tested viruses. The Theralase compound is also effective without activation, but on average, its activation results in a 4.2-fold enhancement of Zika Virus inactivation, a 12-fold enhancement of Influenza inactivation and an 18.7-fold enhancement of CoV inactivation.



Coronavirus Inactivation by Theralase PDC



Human coronavirus OC-43 stocks were treated with 32 µg/mL (PDC)-activator and with indicated concentrations of Theralase PDC® incubated 30 minutes, either activated or not as indicated, and residual virus infectivity determined by immunofocus assay. Horizontal dashed line indicates 50% effective inhibitory dose n=3; error bars are Standard Error of Means

The research is primarily directed to in-vitro (cell lines) analysis, but based on these initial experiments, Theralase® plans to expand the work, in conjunction with Dr. Coombs, to in-vivo (small animal) analysis, toxicology (optimized doses for human delivery), at additional research centers, and if proven successful preclinically, in human clinical testing through Phase I (safety), Phase II (efficacy) and Phase III (efficacy in a larger population) clinical studies. If successful through a Phase III clinical study, and with the successful regulatory approval of Health Canada, the technology could be commercialized across Canada for the benefit of all Canadians.

Note: The Company does not claim or profess that they have the ability to treat, cure or prevent the contraction of the COVID-19 coronavirus.

Intellectual Property Portfolio Growth

Theralase® has received the following decisions to grant a patent:

Country	Patent Title
Russia	Metal-Glycoprotein Complexes and Their use as Chemotherapeutic Compounds
India	Metal-Glycoprotein Complexes and Their use as Chemotherapeutic Compounds
China	Apparatus and Method for Multiwavelength Photo Dynamic Therapy

Metal-Glycoprotein Complexes and Their use as Chemotherapeutic Compounds

This patent is critical in protecting Theralase®'s systemic and targeted anti-cancer therapies to allow PDCs and their associated drug formulations to be systemically injected to “hunt” and “localize” to the cancer cells of interest for various cancer conditions. Once localized in the cancer cells of interest they can be activated by laser light or radiation to destroy the cancer cells safely and effectively.

Apparatus and Method for Multiwavelength Photo Dynamic Therapy

This patent opens new oncological applications, including targeting cancers that are difficult, if not impossible to reach with surgery, such as GBM, a deadly form of brain cancer, NSCLC or other deep tissue related cancers. The multiwavelength PDT system advances the clinical utility of Photo Dynamic Therapy (“PDT”) by expanding the volume of tissue able to be treated. By using various laser light sources to activate the PDCs at differing depths in the target tissue simultaneously or sequentially, Theralase may be able to significantly increase the overall destruction of the cancerous tissue.

Country	Trademark
Canada	Rutherrin®

Rutherrin®

Theralase® has demonstrated that TLD-1433 bonds with transferrin to produce Rutherrin® and in so doing, TLD-1433 is able to be selectively transported, preferentially, and in much higher quantities to cancer cells versus healthy cells through the Transferrin Receptor (“TfR”). Once localized inside a cancer cell, TLD-1433, when light activated, produces a violent form of oxygen, known as singlet oxygen and ROS, that is able to effectively destroy the cancer cell from the inside out through oxidative stress, leading to a natural cell death, known as apoptosis.

Recent Publications

[Optimizing Interstitial Photodynamic Therapy Planning with Reinforcement Learning-Based Diffuser Placement \(Peer reviewed and published on ResearchGate.net\)](#)

ResearchGate is a professional network for scientists and researchers used to share, discover, and discuss research.

Interstitial photodynamic therapy (iPDT) has shown promising results recently as a minimally invasive stand-alone or intra-operative cancer treatment. The development of non-toxic photosensitizing drugs with improved target selectivity has increased its efficacy. However, personalized treatment planning that determines the number of photon emitters, their positions and their input powers while taking into account tissue anatomy and treatment response are lacking to further improve outcomes. New algorithms that generate high-quality plans by optimizing over the light source positions, along with their powers, to minimize the damage to organs-at-risk while eradicating the tumor were developed by using simulated-annealing as a baseline algorithm to place the sources. Algorithms were simulated on virtual brain tumors modeling real glioblastoma multiforme cases, assuming a 5-ALA PpIX induced photosensitizer that is activated at 635 nm wavelength. The algorithm generated plans that achieved an average of 46% less damage to organs-as-risk compared to the manual placement used in current clinical studies. Having a general and high-quality planning system makes iPDT more effective and applicable to a wider variety of oncological indications paving the way for more clinical trials.

This work was supported by Ontario Research Fund, Theralase Technologies Inc., Intel Inc. and International Business Machines (IBM).

(TSXV:TLT.V - OTCQB:TLTFF)