

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.



To date 18 patients have been treated in Study II. The Company has launched 11 Clinical Study Sites in Canada and the US for patient enrollment and treatment under Study II clinical study guideline.

“It is exciting to see Theralase hit its target of having 6 US clinical sites on board in 1Q 2021. It is truly uplifting to be working on the details of getting patients enrolled and treated at these sites. Theralase is another step closer in achieving its next milestone of enrolling and treating 7 additional patients in early 2021 to meet the target of 25 patients for potential Breakthrough Designation.”

**SHAWN SHIRAZI PHD,
CHIEF EXECUTIVE OFFICER, THERALASE®**



OVERVIEW:

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

1. Phase II Non-Muscle Invasive Bladder Cancer (“**NMIBC**”) clinical study for Bacillus Calmette–Guérin (“**BCG**”)–unresponsive Carcinoma In-Situ (“**CIS**”) (“**Study II**”).
2. Glioblastoma Multiforme (“**GBM**”) and Non-Small Cell Lung Cancer (“**NSCLC**”) toxicology studies to allow regulatory submission and approval of a Phase Ib clinical study for both indications.
3. COVID-19 vaccine research and development.

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.

Update on Study II

To date, Theralase® has the following Clinical Study Sites (“CSSs”) open for patient enrollment and treatment:

Clinical Study Sites (Canada)	Location	Commenced
University Health Network (“UHN”)	Toronto, Ontario	April 25, 2019
McGill University Health Centre (“MUHC”)	Montreal, Quebec	July 30, 2019
London Health Sciences Centre (“LHSC”)	London, Ontario	October 7, 2019
Nova Scotia Health Authority (“NSHA”)	Halifax, Nova Scotia	February 25, 2020
University of British Columbia (“UBC”)	Vancouver, British Columbia	December 7, 2020
Virginia Urology (“VU”)	Richmond, Virginia	January 19, 2021
Urology Associates P.C. (“UA”)	Nashville, Tennessee	January 20, 2021
MidLantic Urology (“MU”)	Bala Cynwyd, Pennsylvania	January 25, 2021
Carolina Urologic Research Center (“CURC”)	Myrtle Beach, South Carolina	January 27, 2021
University of Wisconsin Health-Madison (“UWH”)	Madison, Wisconsin	February 24, 2021
Urology San Antonio (“USA”)	San Antonio, Texas	March 25, 2021

Theralase® is currently focused on working with its Canadian and US-based CSSs to enroll and provide the primary Study Treatment for up to 7 additional patients in 2Q2021 for a total of 20 to 25 patients enrolled and treated in Study II. Theralase® plans to compile up to the 90, 180, 270, 360 and 450 day assessment data (urine cytology and cystoscopy) for these patients with the intent of submitting this interim data to the FDA for consideration of Breakthrough Designation (“BTD”) approval.

Patient enrollment and treatment rates have been significantly delayed due to the COVID-19 pandemic restrictions in place at various CSSs; however, they are expected to improve once Canada and the US recover from the COVID-19 pandemic. Canadian CSSs placed themselves on temporary hold commencing March 20, 2020 and resumed normal operations between August 12, 2020 and September 24, 2020. Although Canadian CSSs recruiting activities were re-commenced in 4Q2020; patient recruitment and treatment activities have been severely limited due to the second and third wave of COVID-19. With the addition of 6 additional US-based CSSs in 1Q2021, Theralase® is hopeful that patient recruitment and treatment activities will increase throughout 2021 to help achieve the Company’s strategic objectives.

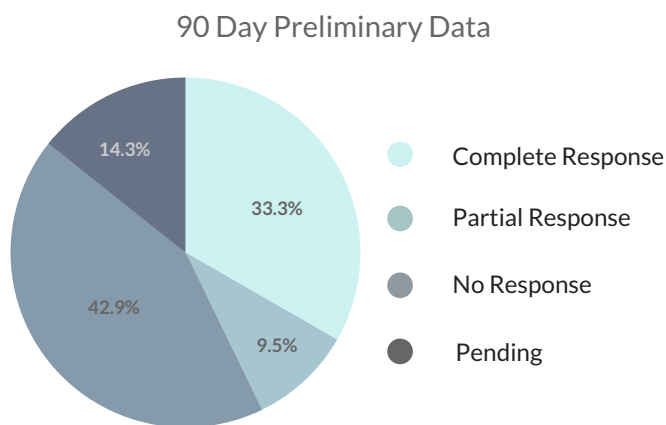
Study II Preliminary Clinical Data

To date, the phase II NMIBC clinical study has enrolled and provided the primary study treatment for 18 patients (including three patients from Phase Ib study treated at the Therapeutic Dose) for a total of 21 patients.

The most recent analysis of the clinical data supports that Study II has met the primary, secondary and tertiary objectives at 180 days post initial Study Treatment, demonstrating a strong initial efficacy, duration of efficacy and high safety profile.

An analysis of the primary (Complete Response (“CR”) at any point in time) and secondary (Duration of CR) objectives, at 90 and 180 days, the CR rate (negative urine cytology and negative cystoscopy) is 33.3% and 28.60%, respectively, while the Partial Response (“PR”) rate (positive urine cytology and negative cystoscopy) is 9.5% and 9.5%, respectively, leading to a 42.8% and 38.10%, Total Response rate (CR and PR), respectively.

Assessment Day	90	%	180	%
Total (Complete Response)*	7	33.3%	6	28.6%
Total (Partial Response)	2	9.5%	2	9.5%
Total Response (CR and PR)	9	42.8%	8	38.1%
Total (No Response)*	9	42.9%	8	38.1%
Total (Pending)	3	14.3%	5	23.8%
Total Treated*	21	100.0%	21	100.0%



* Includes three (3) patients treated at the Therapeutic Dose from the Phase Ib NMIBC Clinical Study (2 - CR and 1 - NR at 90 and 180 Days)

Comparing the 90 and 180 day assessment data, demonstrates that once a patient has obtained CR or PR, the duration of the response remains fairly durable.

In accordance with FDA guidelines to industry, the patients who have achieved a PR are being further assessed via CT scan and biopsy of the prostatic urethra to determine if upper tract Urothelial Cell Carcinoma (“UCC”) or prostatic urethra UCC can be detected to allow these patients to be re-categorized as CR.

In support of the tertiary objective, all patients have experienced some transient grade 1 or grade 2 AEs (e.g.: bladder spasms, constipation, urge incontinence, fatigue, urinary frequency, hematuria, penile discomfort, urinary urgency, pain, urinary tract infections and other) where > 80% have completely resolved with 180 days.

One patient was diagnosed with urosepsis (infection in the urinary tract) that completely resolved within 1 week, after antibiotic treatment and was considered unrelated to the Study Drug, possibly related to the Study Procedure and possibly related to the Study Device, by the PI.

An analysis of the tertiary objective (Adverse Events (“AE”) > 4, that do not resolve within 450 days) showed that 1 patient, who had a negative cytology (no presence of cancer cells in urine) after a single Study Treatment, experienced a grade 3 (Acute Kidney Injury) that was discovered at the 30 day check-up that was considered unlikely related to the Study Drug, probably related to the Study Procedure and possibly related to the Study Device, by the Principal Investigator (“PI”). This same patient, 5 days later, experienced a grade 5 adverse event (Death due to cardiac arrest) that was considered unlikely related to the Study Drug, unlikely related to the Study Procedure and unlikely related to the Study Device, by the PI. The patient had a complex medical history, including diabetes, cardiovascular disease, as well as suffering from benign prostatic hyperplasia. Based on the patient’s history and the timing of the AE, the Company has concluded that both these events were unrelated to the Study Drug and/or Study Device.

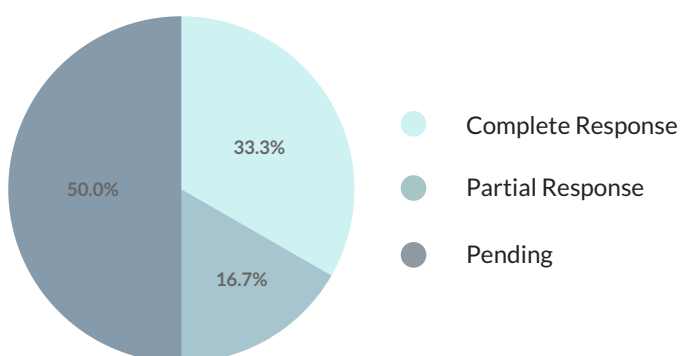
Study II Optimized Treatment Preliminary Results

Commencing August 1, 2020, all new and existing patients to be enrolled and treated (Primary and Maintenance Study Treatments) in Study II were treated using the Study II treatment optimizations as communicated via press release on July 30, 2020, specifically:

1. Bladder volume calculation
2. Study drug volume calculation
3. Study device volume calculation
4. Study device treatment time

In total 6 patients were treated using the Study II treatment optimizations. A preliminary analysis of the primary objective at 90 days for patients receiving the optimized primary Study Treatment demonstrates a 33.3% CR rate, with 50.0% data pending and only 16.7% with no response.

Assessment Day	90	%
Total (Complete Response)	2	33.3%
Total (No Response)	1	16.7%
Total (Pending)	3	50.0%
Total Treated	6	100.0%



Although very early in the data collection and assessment phase, with significant clinical data still to be collected, an interim analysis of the clinical data, for Study Treatments (Primary and Maintenance), completed post August 1, 2020, supports that Study II continues to achieve its primary, secondary and tertiary objectives at 90 days post initial Study Treatment, demonstrating a strong initial efficacy, duration of efficacy and high safety profile.



ACT Research Centre

In April 2021, the Company launched the Theralase® Anti-Cancer Therapy (“ACT”) research center located within the Li Ka Shing Knowledge Institute of St. Michael’s Hospital, Unity Health Toronto, relocating its research team from University Health Network (“UHN”).

The ACT research center is a fully equipped laboratory dedicated exclusively to Theralase® ACT research and development, as Theralase® advances towards commercialization with its lead PDC, TLD-1433, as well as its systemic and targeted formulation – Rutherrin®. A partnership with the Li Ka Shing Knowledge Institute of Unity Health provides access to additional expertise, advisory networks and opportunities to accelerate product development and commercialization.

Additional Oncology Targets

Theralase® has championed the research and development of its Intellectual Property (“IP”) platform for 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)
- Increase ROS production (ability to destroy cancer cells quickly and effectively)
- Increase selective tumour uptake (destruction of cancer cells, while sparing healthy cells) through the Transferrin Receptor (“TfR”)
- Increase anti-cancer efficacy (efficiency in cancer cell destruction)
- Decrease systemic toxicity (damage to healthy cells and/or organs)

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 IP assets regarding its patented PDCs, in pursuit of this goal.

Once Rutherrin®’s Maximum Tolerated Dose (“MTD”) and hence Human Equivalent Dose (“HED”) limits have been determined through non-Good Laboratory Practices (“GLP”) and GLP toxicology studies, Theralase® plans to inject Rutherrin® systemically into patients via a Phase Ib clinical study, planned for 2022, to allow localization to various cancer cells, including Glioblastoma Multiforme (“GBM”) and Non-Small Cell Lung Cancer (“NSCLC”) and then activate Rutherrin® with radiation to safely and effectively, destroy the cancer of interest.

Rutherrin®, if proven successful, would thus be able to “hunt” cancer cells and when activated by radiation “destroy” them; 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.

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.

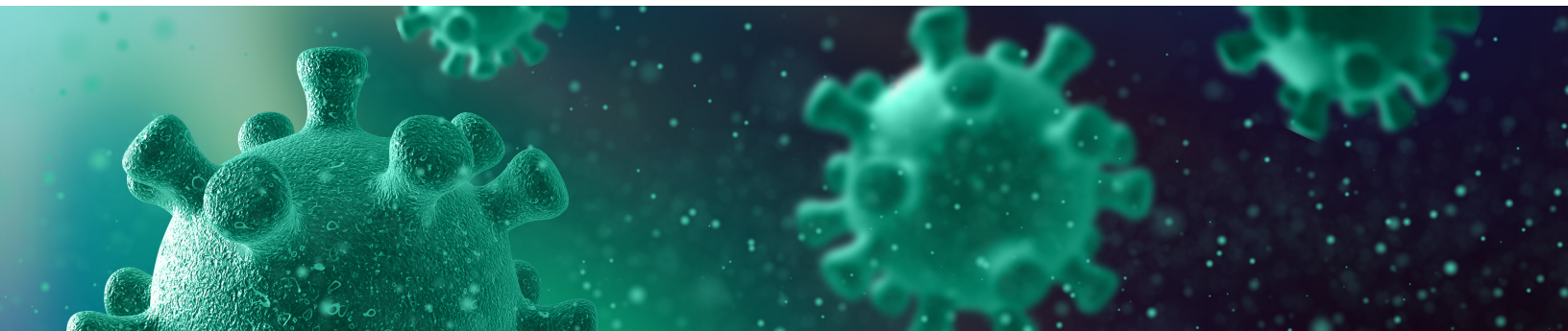


Intellectual Portfolio Growth

Theralase® has been granted a Canadian patent, titled Metal-Based Coordination Complexes as Photodynamic Compounds and their Use.

This invention relates to metal-based coordination complexes that are useful as therapeutic and diagnostic agents. The invention further relates to photodynamic compounds that can be activated with ultraviolet to infrared (UV-IR) light, particularly near infrared light, that are useful as therapeutic and diagnostic agents. In particular, the invention provides tunable metal-based photodynamic compounds that are coordination complexes derived from organic ligands. The photodynamic compounds can be activated by light to destroy unwanted cells, for example hyperproliferative cells and microbial cells. The photodynamic compounds can also be activated by light to destroy viruses.

COVID-19 Vaccine Research



Additional Virus Targets

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).

The Company’s PDC technology was effective in the destruction of Influenza and Zika viruses at low nanomolar concentrations and 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.

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.

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 3.3 nM required to inactivate 50%; whereas; 9.2nM was required to inactivate the same amount of Influenza H1N1 and 12 nM was required to inactivate the same amount of Zika Virus. Similarly, the amount of PDC required to inactivate 99.9% of each virus are 61 nM for CoV, 322 nM for Zika Virus and 497 nM for Influenza H1N1; 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 H1N1 inactivation and an 18.7 fold enhancement of CoV inactivation.

In April 2021, Theralase® executed a Collaborative Research Agreement (“CRA”) with the National Microbiology Laboratory, Public Health Agency of Canada (“PHAC”) for the research and development of a Canadian-based SARS-CoV-2 (“COVID-19”) vaccine. Under the terms of the agreement, Theralase® and PHAC are collaborating on the development and optimization of a Theralase® COVID-19 vaccine by treating the SARS-CoV-2 virus grown on cell lines with Theralase®’s patented PDC and then light activating it with Theralase®’s proprietary TLC-3000A light technology to inactivate the virus and create the fundamental building blocks of a COVID-19 vaccine. This inactivated virus would then be purified and used to inoculate naive animals followed by challenge with the SARS-CoV-2 virus, to ascertain the efficacy of the vaccine. The project is entitled, “Photo Dynamic Compound Inactivation of SARS-CoV-2 Vaccine” and commenced in mid-April 2021.