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## **CORPORATE PRESENTATION**

***The Next Generation Treatment for  
Non-Muscle Invasive Bladder Cancer***

**February 2020**

**TSXV:TLT; OTCQB:TLTFF**

# FORWARD LOOKING STATEMENT



Certain statements contained or incorporated in this presentation, which deal with the financial condition and operating results of Theralase Technologies Inc. ("**Theralase**" or the "**Company**"), include information, analyses and projections as to future corporate developments which are currently in the planning stage and reflect the current expectations of Company's management of the future growth, results of operations, performance, business prospects and opportunities. Such forward-looking statements, made with special reference to the Company's ongoing technologically complex healthcare and medical device research and development efforts include, but are not limited to, assumptions about: the business operations of Theralase continuing on a basis consistent with prior years; the ability of Theralase to access financing from time to time on favourable terms or at all; the continuation of executive management, operating management, key personnel or key consultants or the non-disruptive replacement of them on reasonable terms; the ability of Theralase to maintain reasonably stable operating and general administrative expenses; future success of current research, development and/or commercialization activities of Theralase; the ability of Theralase to achieve development and/or commercial milestones; market competition; the ability of Theralase to secure all necessary regulatory and/or certification approvals; geographic protection over the intellectual property of Theralase in the markets in which Theralase does business; market acceptance and/or revenue generation of Theralase's products under development; the stability of current economic conditions, the strength of the economy in Canada, the United States and elsewhere; currency, exchange and/or interest rates and commodity prices being reasonably stable at current rates. No conclusions as to the successful outcome of the ongoing and planned research and development projects in which the Company is involved are intended or implied nor can they be foreseen or predicted prior to definitive corporate announcements as to their outcome. Any statements that refer to expectations, projections, other characterizations of future events or circumstances are forward-looking statements. Although Theralase believes that the expectations reflected in any forward-looking statements made in this presentation are reasonable, such statements are based on a number of assumptions which may prove to be incorrect; including, but not limited to assumptions related to the risks and factors set out in the Company's current Annual Information Form, available on SEDAR under the Company's profile at [www.sedar.com](http://www.sedar.com). Accordingly, no assurances can be given that any of the events or circumstances contemplated by any such forward-looking statements will transpire or occur or, if any of them transpire or occur, what impact they will have on Theralase's results of operations or financial condition. Furthermore, the forward-looking statements contained in this presentation are made as of the date hereof for the purpose of providing, investors with information regarding the Company's plans for its business and expected milestones. The Company does not undertake any obligation to update publicly or to revise any of the included forward-looking statements, whether as a result of new information, future events, or otherwise, unless required by applicable laws. The forward-looking statements contained in this presentation are expressly qualified by this cautionary statement.

The Company's financial disclosure includes non- International Financial Reporting Standards ("**IFRS**") financial measures as supplemental indicators of the Company's financial and operating performance. The Company believes these supplemental financial measures reflect the Company's on-going business in a manner that allows for meaningful period-to- period comparisons and analysis of trends in its business. Accordingly, the Company believes that such financial measures may also be useful to prospective investors in enhancing their understanding of the Company's operating performance. These non-IFRS measures are not recognized under IFRS and do not have standardized meanings prescribed by IFRS. Therefore, it is unlikely that these measures will be comparable to similarly titled measures reported by other issuers. Non-IFRS financial measures should be considered in the context of the Company's IFRS results. The Company cautions readers to consider these non-IFRS financial measures in addition to, and not as an alternative for, measures calculated in accordance with IFRS. The financial statements of the Company are prepared in accordance with International Financial Reporting Standards and are reported in Canadian dollars. All currency amounts in this presentation are expressed in and all references in this presentation to "\$" to Canadian dollars, unless otherwise indicated.

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## Destroying Cancer at the Speed of Light<sup>™</sup>

- Clinical stage pharmaceutical company
- Focused on the Research & Development of light activated Photo Dynamic Compounds (“**PDCs**”) and the associated drug formulations intended to safely and effectively destroy various cancers.
- Lead cancer indication is Non-Muscle Invasive Bladder Cancer (“**NMIBC**”).
- Medical Laser Technology (“**MLT**”) Division develops, designs, manufactures and commercializes medical laser systems and other technologies for the activation of PDCs.



2011 – 2015

## *Photo Dynamic Therapy*

- In licensed TLD-1433<sup>(1)</sup>
- Began preclinical research with TLD-1433<sup>(2)</sup>

2015 – 2018

## *Clinical Phase 1*

- Completed Phase Ib NMIBC clinical study<sup>(3)</sup>
  - 67% Complete Response (“**CR**”) at 540 days for the Therapeutic Dose (0.70mg/cm<sup>2</sup>) (2 out of 3 patients)<sup>(3)</sup>
- US composition of matter patent for Metal-Based Thiophene Photodynamic Compounds and Their Use<sup>(4)</sup> (TLD-1433)

2019 – 2022

## *Clinical Phase 2*

- Phase II NMIBC clinical study commenced<sup>(5)</sup>
- Appointment of Chief Executive Officer<sup>(6)</sup>
- Health Canada regulatory approvals<sup>(7)(8)</sup>
- CAD\$ 17,250,000 financing<sup>(9)</sup>
- FDA IND submission

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<sup>(1)</sup> McFarland – Theralase Licence Agreement, Dated: September 11, 2011

<sup>(2)</sup> University Health Network – Theralase Sponsored Research Agreement Dated: Licenc Agreement, Dated: May 1, 2014 (UHN Ref.#: 2014-0288)

<sup>(3)</sup> Theralase Press Release “Patient Six Cancer-Free Twelve Months After Single Anti-Cancer Treatment, Results of Phase Ib Non-Muscle Invasive Bladder Cancer (“**NMIBC**”) Clinical Study Demonstrate a 66% Complete Response (“**CR**”) at the Therapeutic Dose (0.70 mg/cm<sup>2</sup>) 360 Days Post Treatment”, Dated: April 2, 2019

<sup>(4)</sup> U.S. Patent Nos. 9,345,769 and 9,676,806 and Canadian Patent No. 2,883,068 patents for “Metal-Based Thiophene Photodynamic Compounds and Their Use”

<sup>(5)</sup> Theralase Press Release “Theralase Commences Phase II NMIBC Clinical Study”, Dated: April 25, 2019

<sup>(6)</sup> Theralase Press Release “Theralase Announces Appointment of New Chief Executive Officers”, Dated: February 25, 2019

<sup>(7)</sup> Theralase Press Release “Health Canada Grants ITA Approval to Commence Phase II Clinical Study” Dated December 10, 2018

<sup>(8)</sup> Theralase Press Release “Health Canada Approves Commencement of Phase II Clinical Study” Dated September 10, 2018

<sup>(9)</sup> Theralase Press Release “Closing of Prospectus Offering for Gross Proceeds of \$17,250,000” Dated August 22, 2019

# INVESTMENT HIGHLIGHTS



## OVERSUBSCRIBED PROSPECTUS OFFERING

The Company successfully completed an oversubscribed marketed public offering on August 22, 2019, raising gross proceeds of CAD \$17,250,000.

## SUCCESSFUL PHASE IB NMIBC CLINICAL STUDY

The study results have shown a strong efficacy signal with a 67% CR after only a single treatment, with patients five and six demonstrating cancer-free status with no presence, recurrence or progression of the disease, 540 days post initial treatment. <sup>(3)</sup>

## STRONG MANAGEMENT TEAM

Seasoned management with pharmaceutical and medical device experience

## PHASE II CLINICAL STUDY LAUNCH

The commencement of Study II is underway with two patients treated at the Company's lead study site, University Health Network ("**UHN**") in Toronto. <sup>(10)</sup>

## FDA COMPLIANCE

In June 2019, FDA confirmed in a Pre-Investigational New Drug ("**IND**") conference call, that Theralase's protocol design for Study II was aligned with the industry guidelines (February, 2018) for Bacillus Calmette Guerin ("**BCG**")-Unresponsive NMIBC. In September 2019, Theralase submitted IND to FDA. <sup>(11)</sup>

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<sup>(10)</sup> Theralase Press Release "London Health Sciences Centre Launches as Newest Clinical Study Site for Phase II Non-Muscle Invasive Bladder Cancer Clinical Study" Dated Oct 7, 2019

<sup>(11)</sup> Theralase Press Release "Theralase Files Investigational New Drug Application with the FDA" Dated Oct 1, 2019

# EXPERIENCED LEADERSHIP TEAM



**Shawn Shirazi**  
**PhD**

***CEO***

**20+ years in Drug Development,  
Clinical studies, GMP Mfg.**

- 20+ years of hands-on experience in pharmaceutical drug formulation and development, clinical trial management, Good Manufacturing Practices (“GMP”) international drug manufacture, international regulatory guidelines and quality assurance in GMP drug manufacture
- He has held senior roles with both start-ups and large pharmaceutical organizations
- Led the generic drug development programs for numerous pharmaceutical organizations, resulting in multiple “First To File” drug applications



**Arkady Mandel**  
**MD, PhD, DSc**

***Chief Scientific Officer***

**25+ years in Technology  
Creation, Invention, Innovation**

- One of the key founders of the therapeutic use of laser in dermatology and other areas of clinical medicine
- Over 100 original papers and scientific monographs to his name, combined with over 200 international patents
- Earned his designation as a medical doctor from the Moscow State Medical University
- Doctor of Science accreditation majoring in biochemistry, microbiology, immunology, biophysics and photobiology



**Kristina Hachey**  
**CPA**

***Chief Financial Officer***

**20+ years in Finance &  
Operations**

- 20+ years of experience in finance and financing for public and private companies
- Chief Financial Officer of Theralase and Theralase Technologies Inc. since May 2004
- VP Finance of Kensington Capital Partners from April 1998 to May 2004
- Graduated from Ryerson University with a bachelor degree in Business Management and Administration, majoring in Accounting and Finance, minoring in International Business

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# MEDICAL AND SCIENTIFIC ADVISORS



**Michael Jewett  
MD**

*UHN, Chair of MSAB*

- Professor of surgery (urology) at University of Toronto, surgical oncology at Princess Margaret Cancer Centre, University Health Network
- Clinical practice is in urologic oncology with research interests in testicular cancer and superficial bladder cancer



**Ashish M. Kamat  
MD**

*MD Anderson*

- Internationally recognized expert in urologic oncology and authority in the management of urologic cancers with expertise in bladder cancer, organ sparing and minimally invasive techniques
- Maintains an active research portfolio with focus on efforts to develop novel therapies and identify predictors of response to therapy
- Initiated, led and active in several large studies including multinational trials in bladder cancer, findings published in high impact journals



**Michael O'Donnell  
MD**

*University of Iowa*

- Long history of focusing on bladder immunology and bladder cancer immunotherapy, particularly the anti-cancer mechanism of bacillus calmette-Guerin ("BCG") and its enhancement with combination therapies
- Recently headed a national trial of bladder cancer treatment utilizing BCG plus interferon (a natural protein which induces health cells to combat disease) comprised of over 1,000 patients and holds several US patents for his work



**Lothar Lilge  
PhD**

*UHN*

- Professor in the Department of Medical Biophysics, University of Toronto and Senior Scientist at the Ontario Cancer Institute, UHN
- Research is focused on photo dynamic therapy, optical diagnostics, destruction of cancer and bacteria by light activated PDC's and the use of light as a microscopic tool for biomedical research



**Brian Wilson  
PhD**

*UHN*

- Senior Scientist and Head of the Applied Biophotonics group at UHN
- Professor in the Department of Medical Biophysics at the University of Toronto
- Research focus of the Applied Biophotonics group is the development and application of new therapeutic and diagnostic techniques based on the use of lasers and other optical technologies

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# NON-MUSCLE INVASIVE BLADDER CANCER ("NMIBC")

**240,000**

new cases of bladder cancer each year in the U.S., Canada and Europe<sup>(12)</sup>

**70%**

of all new cases are classified as NMIBC<sup>(13)</sup>

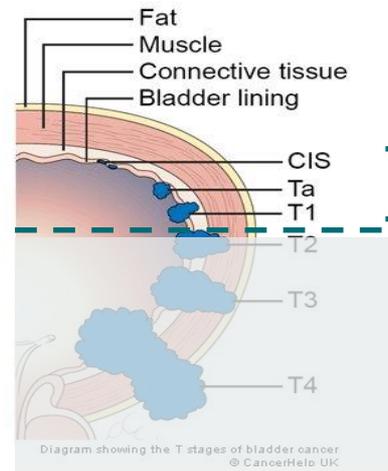
**30%**

of these cases become unresponsive ("BCG-Unresponsive") to current standard of care treatment within 1 year<sup>(14)</sup>

## Current Treatment Guidelines

- Standard of care for patients with high-grade NMIBC remains intravesical BCG following Trans Urethral Resection of the Bladder Tumour ("TURBT"). With up to **80% rate of tumour recurrence and up to 50% progression within 5 years**<sup>(15)</sup>
- Over 30 years since a new drug has been approved for NMIBC, BCG-Unresponsive patients.
- When patients fail to respond to current standard of care, U.S. treatment guidelines call for a radical cystectomy (surgical removal of the bladder and adjacent organs)<sup>(16)</sup>

## Stages of Bladder Cancer



**Theralase's lead cancer indication is Non-Muscle Invasive Bladder Cancer**

Once papillary cancer has grown into the muscle wall beneath the bladder lining, it is referred to as Muscle Invasive Bladder Cancer ("MIBC")

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<sup>(12)</sup> Key Statistics for Bladder Cancer – American Cancer Society (2018); Canadian Cancer Society (2017) and Bladder Cancer Incidence Statistics – Cancer Research UK

<sup>(13)</sup> <https://www.uptodate.com/contents/bladder-cancer-treatment-non-muscle-invasive-superficial-cancer-beyond-the-basics#>

<sup>(14)</sup> The management of BCG failure in non-muscle-invasive bladder cancer: an update (2009)

<sup>(15)</sup> European Organization for Research and Treatment of Cancer (EORTC) - (Veeratterapillay R, Heer R, Johnson MI, Persad R, Bach C. High-risk non-muscle-invasive bladder cancer-therapy options during intravesical BCG Shortage. Curr Urol Rep. 2016;17:68) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5769243/>

<sup>(16)</sup> NCCN Guidelines Insights: Bladder Cancer, Version 5.2018, J Natl Compr Canc Netw 2018;16(9):1041–1053

# LARGE MARKET OPPORTUNITY



*(all figures in \$U.S.)*



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<sup>(17)</sup> Willingness to pay per quality adjusted life year (QALY) for competitor drug, Pembrolizumab. Source: Cost-effectiveness of Pembrolizumab in Second-line Advanced Bladder Cancer, July 2018

<sup>(18)</sup> 2025 estimated bladder cancer market (US, France, Germany, Italy, Spain, UK & Japan). Source: Global Data: Bladder cancer market size to more than triple to over \$1.1 billion by 2025, April 2017

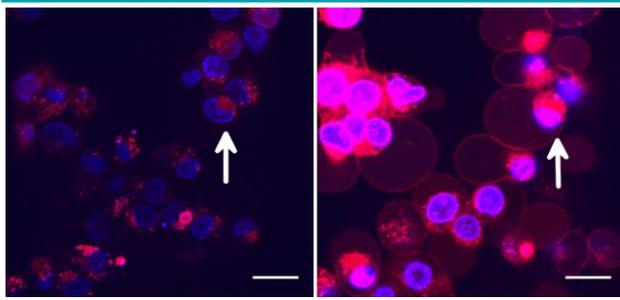
# THERALASE'S PHOTO DYNAMIC THERAPY SOLUTION



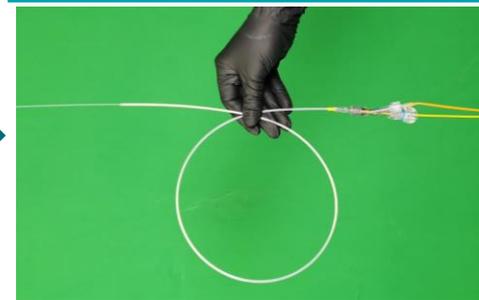
## Patented PDC drug is TLD-1433, (Laser light activated for the treatment of NMIBC)

- Laser light activated (Theralase TLC-3200 System)
- NMIBC cells destroyed through the production of Reactive Oxygen Species and singlet oxygen
- Performed as an outpatient day surgery procedure

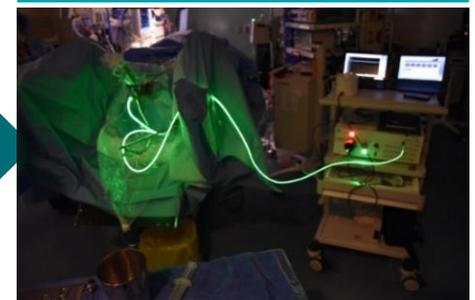
**TLD-1433<sup>(19)</sup>  
Localized to Bladder  
Cancer Tumors**



**Theralase TLC-3200 System  
(Laser Emitter and Laser  
Detector)**



**Photo Dynamic Therapy  
Treatment Procedure**



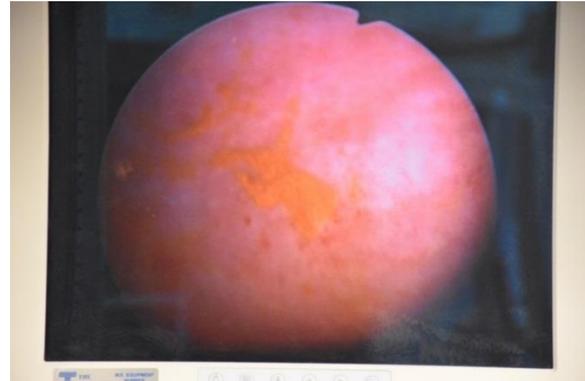
**Seeking regulatory approval for drug / device combination as an alternative for patients who are unfit for cystectomy or desire bladder-preserving therapies**

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# PDT TREATMENT PROCEDURE<sup>(20)</sup>

1. Study Drug (TLD-1433) reconstituted in pharmacy up to 24 hours prior to treatment procedure
2. Catheter inserted through urethra and Study Drug instilled intravesically into bladder for approximately 60 minutes
3. Patient taken to operating room, where bladder is voided and patient undergoes general anesthetic
4. Cystoscope inserted through urethra into bladder
5. Bladder rinsed with sterile water via cystoscope to remove excess PDC
6. Bladder distended using instillation of sterile water to prevent folds that prevent uniform light illumination
7. Emitter and Detector inserted through working channel of flexible cystoscope and positioned in bladder with the aid of diagnostic ultrasound
8. Bladder illuminated with green laser light to ensure placement and then full power initiated
9. TLC-3200 measures light delivery in real time, allowing for treatment interruptions (i.e.: bladder irrigations, fiber positioning) while helping to ensure that the laser light energy density delivered to the bladder wall is approximately 90 J/cm<sup>2</sup>

**Human Bladder Post Rinse Showing TLD-1433 Localized to Bladder Cancer Tumours**



**Preferential accumulation of Study Drug in the NMIBC tumour regions of the bladder wall post wash<sup>(21)</sup>**

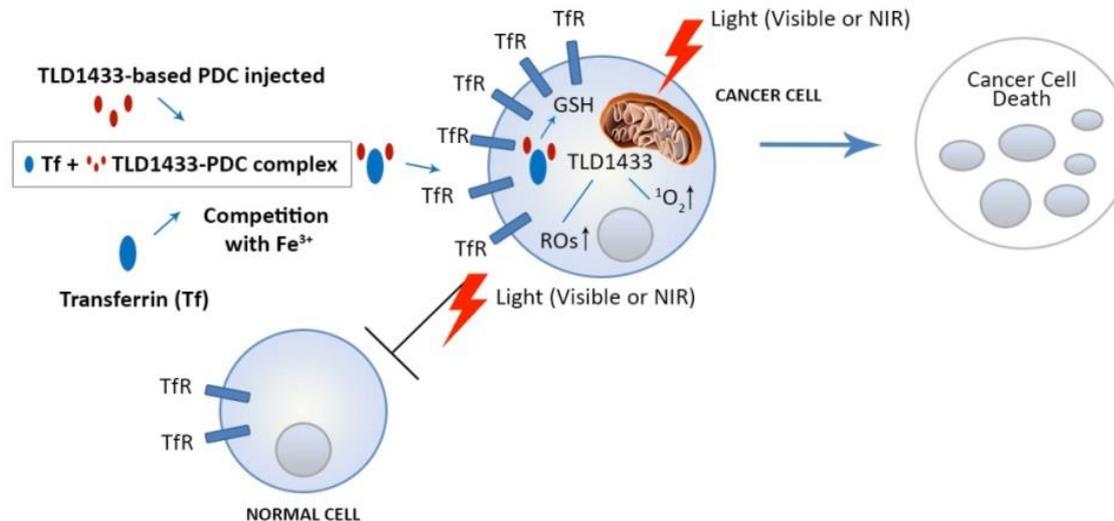
**Transferrin receptors not detected on normal urothelium. Positive staining was found to increase with increased pathological grade and stage of the tumours<sup>(22)</sup>**

<sup>(20)</sup> Clinical Protocol TLD-1433-2 (Version 8.0) Dated: April 16, 2019

<sup>(21)</sup> Phase Ib NMIBC Clinical Study patient cystoscopy photograph, after instillation of Study Drug, prior to TLC-3200 Light Activation

<sup>(22)</sup> Reference: Urol Res. 1987;15(6):341-4. Transferrin receptor expression by human bladder transitional cell carcinomas, Seymour GJ, Walsh MD, Lavin MF, Strutton G, Gardiner RA

## TLD-1433 + Transferrin = Rutherrin<sup>®</sup>



■ TfR = Transferrin receptor

- Transferrin transports molecular Iron to every cell in the body
- Ruthenium is a transition metal having similar properties to Iron. TLD-1433 is a Ruthenium based compound binding to transferrin to form Rutherrin<sup>®</sup>.
- Cancer cells have a larger number of transferrin receptors versus healthy cells. <sup>(24)(25)</sup>
- Rutherrin<sup>®</sup> is preferentially attracted to a wide variety of cancer cells, allowing TLD-1433 to cross the cancer cell membrane and, when light activated, produce powerful cytotoxins in the form of Reactive Oxygen Species and singlet oxygen.

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<sup>(23)</sup> Kaspler P, Lazic S, Forward S, Arenas Y, Mandel A, Lilje L. A ruthenium(ii)based photosensitizer and transferrin complexes enhance photo-physical properties, cell uptake, and photodynamic therapy safety and efficacy. Photochem Photobiol Sci. 2016 Apr;15(4):481-95. doi: 10.1039/c5pp00450k. Epub 2016 Mar 7. PubMed PMID: 26947517.

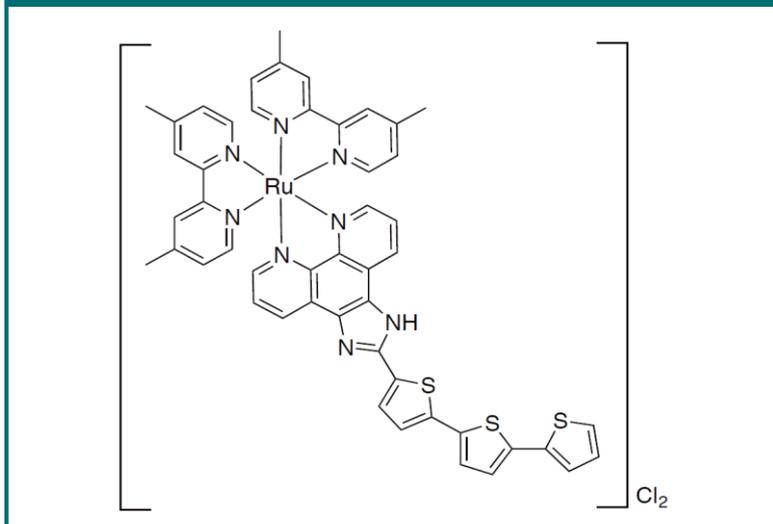
<sup>(24)</sup> Transferrin receptor regulates pancreatic cancer growth by modulating mitochondrial respiration and ROS generation. Jeong SM, Hwang S, Seong RH

<sup>(25)</sup> A novel transferrin receptor-targeted hybrid peptide disintegrates cancer cell membrane to induce rapid killing of cancer cells. Megumi Kawamoto, Tomohisa Horibe, Masayuki Kohno, Koji Kawakami

# INTELLECTUAL PROPERTY & PUBLICATIONS

- U.S. composition of matter patent expires in June 2034<sup>4</sup>
- 12 issued patents<sup>(26)</sup>
- 34 patents filed in various stages of approval (pending, published & allowed) in U.S., Canada and International<sup>(26)</sup>

TLD-1433 Chemical Structure



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<sup>(26)</sup> Theralase Annual Information Form for the Year End December 31, 2018, Dated April 25, 2019

# PHASE Ib CLINICAL STUDY

Successfully completed a Phase Ib NMIBC clinical study<sup>(3)</sup>

- 3 patients at Maximum Recommended Starting Dose (0.35 mg/cm<sup>2</sup>)
- 3 patients at Therapeutic Dose (0.70 mg/cm<sup>2</sup>)

## Primary

Safety and tolerability measured by Adverse Events ("AEs") not resolved within 180 days

## Secondary

Pharmacokinetics (movement and exit of drug within tissue), measured using plasma and urine samples

## Exploratory

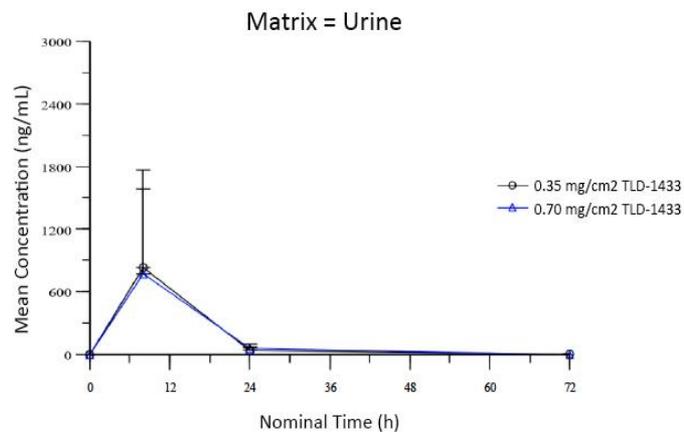
Efficacy (evaluated primarily at 90 days, secondarily at 180 days), measured by Recurrence Free Survival ("RFS")

## Primary - Safety

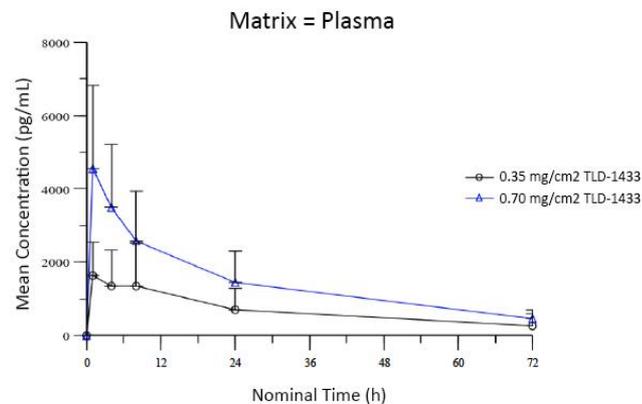
- Strong safety profile
- 95% of AEs completely resolved within 180 days
- 5% of AEs not completely resolved were not related to study drug

## Secondary – Pharmacokinetics<sup>(27)</sup>

Concentration of TLD-1433 in Urine Versus Time



Concentration of TLD-1433 in Plasma Versus Time



TLD-1433 is predominantly removed from the body via urine within 24 hours and via plasma within 72 hours. No photosensitivity issues.

## Exploratory - Efficacy

- 67% Complete Response ("CR") treated with one therapeutic dose (0.70 mg/cm<sup>2</sup>) at 540 days post treatment (2 out of 3 patients)

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# PROMISING CLINICAL RESULTS<sup>(28)</sup>

Subject	001-001 (Patient 1)	001-002 (Patient 2)	001-003 (Patient 3)	001-004 (Patient 4)	001-005 (Patient 5)	001-006 (Patient 6)
Treatment Dose	MSRD (0.35mg/cm <sup>2</sup> )	MSRD (0.35mg/cm <sup>2</sup> )	MSRD (0.35mg/cm <sup>2</sup> )	Therapeutic Dose (0.70mg/cm <sup>2</sup> )	Therapeutic Dose (0.70mg/cm <sup>2</sup> )	Therapeutic Dose (0.70mg/cm <sup>2</sup> )
Pathology	T1 HG w/ Cis (180 days)  <b>No disease progression (180 days)</b>	T1 HG w/Cis (180 days)  <b>No disease progression (180 days)</b>	Cis (180 days)  <b>No disease progression (180 days)</b>	T1 HG w/ Cis Unrelated to Treatment (138 days)	<b>No clinical evidence of bladder tumour (540 days)</b>	<b>No clinical evidence of bladder tumour (540 days)</b>
Imaging	Increased lymphadenopathy Generalized bladder wall thickening, and dilation of the right greater than left ureter again seen. Again noted is an area of ureteric thickening and narrowing on the right side (180 Days)	Solid mass in the right renal pelvis has enlarged in the interval (180 Days)	No definite evidence for abdominal pelvic disease. Plaque-like areas of calcification in the posterior bladder wall grossly similar (180 Days)	1) Vertebral metastases 2) Focus of density within the left upper pole renal calyx is likely intra - pelvis urothelial malignancy  Patient removed from study (138 Days)	<b>540 Day Cystoscopy: No clinical evidence of bladder tumour (540 Days)</b>  <b>No evidence of metastatic disease in the abdomen or pelvis.</b>	<b>540 Day Cystoscopy: No clinical evidence of bladder tumour (540 Days)</b>  <b>No evidence of metastatic disease in the abdomen or pelvis.</b>

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<sup>(28)</sup> Princess Margaret Cancer Centre, University Health Network (2017 to 2019)

# PHASE II CLINICAL STUDY



## ACT (Anti-Cancer Treatment) – NMIBC

Multi-site (Approximately 20 sites)  
single-arm, open-label study

Approximately 100 patients to be  
evaluated at Therapeutic Dose (0.70  
mg/cm<sup>2</sup>)

All patients to receive two treatment procedure (Day 0 and Day 180)<sup>(29)</sup>

### Key Inclusion Criteria

- Histologically confirmed NMIBC Carcinoma In-Situ (“**CIS**”) with resected papillary disease (Ta, T1) (high grade) via TURBT that are BCG-Unresponsive<sup>(30)</sup>

**FDA guidelines (February 2018) for BCG-Unresponsive Non Muscle Invasive Bladder Cancer states that:**

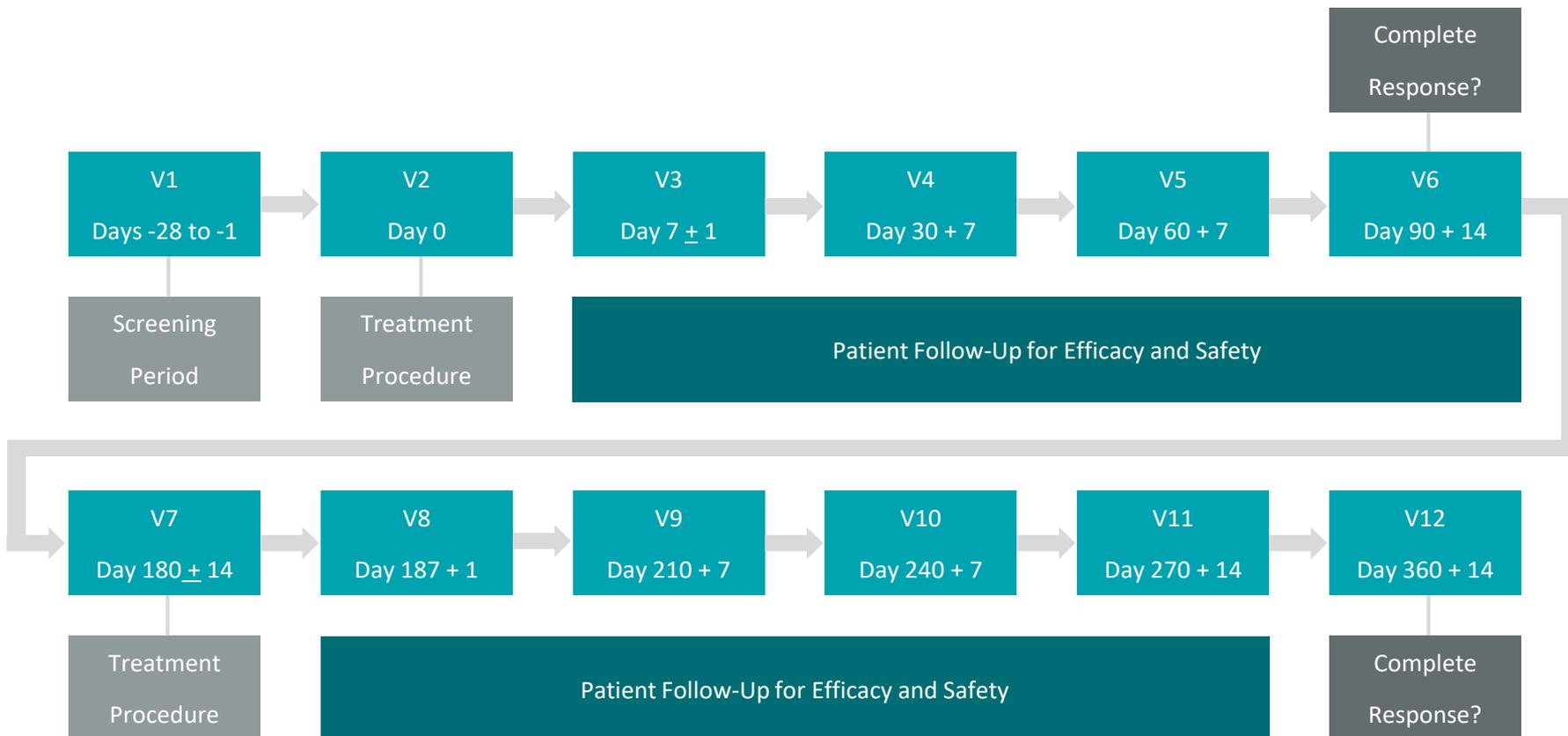
***“In BCG-unresponsive NMIBC, a single-arm clinical trial with Complete Response rate and duration of response as the primary endpoint can provide primary evidence of effectiveness to support a marketing application”<sup>(30)</sup>***

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<sup>(29)</sup> Clinical Protocol TLD-1433-2 (Version 8.0) Dated: April 16, 2019

<sup>(30)</sup> “BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment - Guidance for Industry” Dated: February 2018

# PHASE II CLINICAL STUDY DESIGN



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# ACT-NMIBC OUTCOME MEASURES



## Primary Outcome Measure<sup>(30)</sup>

Evaluated by Complete Response (“**CR**”) at 90 days post-treatment and duration of CR evaluated at approximately 360 days post-treatment.

### **CR defined as being one of the following:**

- Negative cystoscopy and negative urine cytology; or
- Positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative cytology; or
- Negative cystoscopy with malignant urine cytology if cancer is found in the upper tract or prostatic urethra and random bladder biopsies are negative.

## Secondary Outcome Measure

The safety is evaluated by the incidence and severity of Adverse Events Grade 4 or higher that do not resolve within 360 days post-treatment.

Grade 1 = Mild

Grade 2 = Moderate

Grade 3 = Severe

Grade 4 = Life-threatening or disabling

Grade 5 = Death

# COMPETITION



Year Clinical Study Completed	Drug	Efficacy (CR ≥30% at 12 months)	Safety (Adverse Events (AEs)) > Grade 2	Status
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## Current Studies

Ongoing (phase II)	<b>TLD-1433 (Theralase)<sup>(3)</sup></b>	CR = 67% at 18 months	No	Phase II to commence Q2 2019
Ongoing (phase II)	Oncolytic adenovirus (CG0070 virus) <sup>(31)</sup>	CR = 27% at 12 months	Yes	Phase II underway
Ongoing (phase III)	Vicinium (VB4-845) <sup>(32)</sup>	CR = 15% at 12 months	Yes	Phase III underway
Ongoing (phase III)	Recombinant Adenovirus (Interferon-α2b(rAd-IFN)) <sup>(33)</sup>	35% Recurrence-Free Survival (RFS) at 12 months	Yes	Phase III underway
Expected 2023	PD-1 / PD-L1 checkpoint inhibitors (Atezolizumab, durvalumab, avelumab, nivolumab, and pembrolizumab) <sup>(34)</sup>	CR = 38.8% at 3 months	Yes	Approved for patients w/metastatic and locally-advanced bladder cancer (not approved for NMIBC). FDA halted 2 studies due to decreased patient survival with low expression levels of PD-L1 versus platinum-based chemotherapy.

## Completed Studies

2007	Doxorubicin / Epirubicin <sup>(33)</sup>	CR = 35% at 14 to 31 days	Yes	Approved / Not used in clinical practice
2011	Gemcitabine <sup>(35)</sup>	CR = 10% at 12 months	Yes	Approved / Not used in clinical practice
2012	Electromotive Mitomycin-C <sup>(36)</sup>	CR = 58% at 6 months	Yes	Approved / Not currently available in the US
2014	Thiotepa <sup>(37)</sup>	CR = 52% at 4.2 months	Yes	Approved / Not used in clinical practice
2015	Mycobacterium phlei cell wall-nucleic acid complex (MCNA) <sup>(38)</sup>	Disease Free Survival (DFS) = 25% at 12 months	Yes	Not approved
2017	Valrubicin <sup>(39)</sup>	CR = 18% at 6 months	Yes	Approved / Not used in clinical practice

Meets Criteria

May Meet Criteria

Does Not Meet Criteria

<sup>(31)</sup> AUA 2018: CG0070, an Oncolytic Adenovirus, for BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer: 12 Month Interim Results from a Multicenter Phase II Trial (<https://www.urotoday.com/conference-highlights/aua-2018/aua-2018-bladder-cancer/104383-aua-2018-cg0070-an-oncolytic-adenovirus-for-bcg-unresponsive-non-muscle-invasive-bladder-cancer-12-month-interim-results-from-a-multicenter-phase-ii-trial.html>)

<sup>(32)</sup> Sesen Bio Reports First Quarter 2019 Financial Results and Updated, Preliminary Primary and Additional Secondary Endpoint Data from Phase 3 VISTA Trial for High-Risk Non-Muscle Invasive Bladder Cancer (ir.sesenbio.com/news-releases/news-release-details/sesen-bio-reports-first-quarter-2019-financial-results-and)<sup>30</sup> Gene Therapy Shows Promise For Bladder Cancer Subtype (<https://www.healio.com/hematology-oncology/genitourinary-cancer/news/in-the-journals/%7B09ac04a0-4445-4189-8175-9f3ca3c8e892%7D/gene-therapy-shows-promise-for-bladder-cancer-subtype>)

<sup>(33)</sup> Keytruda Elicits Complete Response in 40% of Group of High-risk Bladder Cancer Patients, Early Phase 2 Trial Data Show (<https://immuno-oncologynews.com/2018/11/09/keytruda-elicits-complete-response-in-40-percent-of-high-risk-bladder-cancer-patient-group-early-phase-2-trial-data-show/>)

<sup>(34)</sup> Intravesical epirubicin versus doxorubicin for superficial bladder tumors (stages pTa and pT1): a randomized prospective study (<https://www.ncbi.nlm.nih.gov/pubmed/9186325?dopt=Abstract>)

<sup>(35)</sup> Intravesical gemcitabine for non-muscle invasive bladder cancer (<https://www.ncbi.nlm.nih.gov/pubmed/22259002?dopt=Abstract>)

<sup>(36)</sup> Management of carcinoma *in situ* of the bladder: best practice and recent developments (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4647140/>)

<sup>(37)</sup> Thiotepa versus Bacille Calmette-Guérin in Non-Muscle Invasive Bladder Cancer (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3783275/>)

<sup>(38)</sup> Efficacy and Safety of MCNA in Patients with Non-Muscle Invasive Bladder Cancer at High-Risk of Recurrence and Progression who Have Failed Treatment with Bacillus Calmette-Guérin

[https://www.researchgate.net/publication/266562521\\_Efficacy\\_and\\_Safety\\_of\\_MCNA\\_in\\_Patients\\_with\\_Non-Muscle\\_Invasive\\_Bladder\\_Cancer\\_at\\_High-Risk\\_of\\_Recurrence\\_and\\_Progression\\_who\\_Have\\_Failed\\_Treatment\\_with\\_Bacillus\\_Calmette-Guerin](https://www.researchgate.net/publication/266562521_Efficacy_and_Safety_of_MCNA_in_Patients_with_Non-Muscle_Invasive_Bladder_Cancer_at_High-Risk_of_Recurrence_and_Progression_who_Have_Failed_Treatment_with_Bacillus_Calmette-Guerin)

<sup>(39)</sup> Intravesical valrubicin in patients with bladder carcinoma *in situ* and contraindication to or failure after bacillus Calmette-Guérin (<https://www.ncbi.nlm.nih.gov/pubmed/22575238>)

# ADVANTAGE



## TWO AND DONE

Two outpatient day surgery procedures<sup>(29)</sup>

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## EFFICACY

Strong efficacy signal<sup>(3)</sup> (67% Complete Response at 540 days post treatment)

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## REGULATORY FAST TRACK

Potential for fast track designation

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## COMMERCIALIZATION

Successful Phase II results could support marketing application

Kalinina, Sviatlana; Breymayer, Jasmin; Reess, Kirsten; et al. [Correlation of intracellular oxygen and cell metabolism by simultaneous PLIM of phosphorescent TLD1433 and FLIM of NAD\(P\)H](#) Journal of biophotonics Pages: e201800085: 2018

Kaspler, Pavel; Lazic, Savo; Forward, Sarah; et al. [A ruthenium\(II\) based photosensitizer and transferrin complexes enhance photo-physical properties, cell uptake, and photodynamic therapy safety and efficacy](#) PHOTOCHEMICAL & PHOTOBIOLOGICAL SCIENCES 15:481-495: 2016

Fong, Jamie; Kasimova, Kamola; Arenas, Yaxal; et al. [A novel class of ruthenium-based photosensitizers effectively kills in vitro cancer cells and in vivo tumors](#) PHOTOCHEMICAL & PHOTOBIOLOGICAL SCIENCES 14:2014-2023: 2015

Shi, Ge; Monro, Susan; Hennigar, Robie; et al. [Ru\(II\) dyads derived from alpha-oligothiophenes: A new class of potent and versatile photosensitizers for PDT](#) COORDINATION CHEMISTRY REVIEWS 282:127-138: 2015

Reichardt, Christian, Mitch Pinto, Maria Wächtler, Mat Stephenson, Stephan Kupfer, Tariq Sainuddin, Julien Guthmuller, Sherri A. McFarland, and Benjamin Dietzek. 2015. "[Photophysics of Ru\(II\) Dyads Derived from Pyrenyl-Substituted Imidazo\[4,5-f\]\[1,10\]phenanthroline Ligands](#)" *The Journal of Physical Chemistry. A* 119 (17): 3986–94. doi:10.1021/acs.jpca.5b01737.

Yin, Huimin, Mat Stephenson, Jordan Gibson, Eric Sampson, Ge Shi, Tariq Sainuddin, Susan Monro, and Sherri A. McFarland. 2014. "[In Vitro Multiwavelength PDT with 3IL States: Teaching Old Molecules New Tricks](#)" *Inorganic Chemistry* 53 (9): 4548–59. doi:10.1021/ic5002368.

## PEER REVIEWED PUBLICATIONS (CONTINUED)



Monro S; Colon KL; Roque J; et al. [Transition Metal Complexes and Photodynamic Therapy from a Tumor-Centered Approach: Challenges, Opportunities, and Highlights from the Development of TDL1433](#) *Chem Rev*, 2018 Oct 8. doi: 10.1021/acs.chemrev.8b00211

Yassine AA; Lilge L; Betz V. [Optimizing interstitial photodynamic therapy with custom cylindrical diffusers](#) *J Biophotonics*, 2019 Jan 12(1):e201800153. doi: 10.1—2/jbio.201800153

Thota S; Rodrigues DA; Crans DC; Barreiro EJ. [Ru\(II\) Compounds: Next-Generation Anticancer Metallotherapeutics?](#) *J Med Chem*, 2018 Feb 26 doi: 10.1021/acs.jmedchem.7b01689

Zhang SQ; Geo LH; Zhao H; Wang KZ. [Recent Progress in Polynuclear Ruthenium Complex-Based DNA Binders/Structural Probes and Anticancer Agents](#) *Curr Med Chem* 2018 Dec 3 doi: 10.2174/0929867326666181203143422