Theralase Therapeutic Laser Technology Enhances Cancer Destruction

Toronto, Ontario – November 27, 2017, Theralase Technologies Inc. (“Theralase®” or the “Company”) (TSXV: TLT) (OTCQX: TLFF), a leading biotech company focused on the commercialization of medical lasers to eliminate pain and the development of Photo Dynamic Compounds (“PDCs”) to destroy cancer has announced that its Theralase® therapeutic laser technology platform has been proven preclinically to render cancer cells more susceptible to cancer destruction by Photo Dynamic Therapy (“PDT”), by reversing the Warburg Effect.

One of the hallmarks of cancer cells is a change in cellular metabolism from mitochondrial respiration (the production of Adenosine TriPhosphate (“ATP”)) that relies on oxygen consumption to glycolysis, an oxygen independent process.

Cancer cells systematically modify their metabolism to promote their: growth, survival, proliferation and long-term maintenance, without the need for molecular oxygen, thus making them difficult to destroy by traditional means.

This common feature, amongst cancer cells, of a modified metabolism, is demonstrated by an increase in glucose (blood sugar) uptake and an increase in lactate production. This phenomenon was originally described by Dr. Otto Warburg at the turn of the 19th century, where he was awarded the Nobel prize in physiology or medicine for his work, and has subsequently been suitably named as the “Warburg Effect.”

The Warburg Effect describes cancer cells that are characterized by their decreased mitochondrial respiration, increased glycolysis (production of ATP without the use of molecular oxygen) and excessive lactate production.

Theralase’s TLC-2000 Cold Laser Therapy (“CLT”) was used to irradiate both in vitro GlioBlastoma Multiforme (“GBM”) Rat Glioma (“RG2”) brain and also transitional cell carcinoma bladder cancer cells (T24). The data below is for GBM RG2 cancer cells, but the CLT treatment of human bladder cancer cells rendered similar results on the Warburg Effect (data not shown)

Post treatment analysis of both of these cancer cell lines demonstrated a 20% decrease in the glycolysis rate (measured by a decrease in lactate production) and a 20% increase in mitochondrial respiration, leading to a shift in their metabolism (from cancerous to normal), indicating a reversal of the aptly named, Warburg Effect.
During the transformation of cells from normal existence to cancerous, the Warburg Effect is associated with numerous metabolic gene expressions necessary for glycolysis, such as, the upregulation of:

1) Glucose Transporter 1 ("GLUT1") (used to increase glucose uptake and the glycolysis rate)
2) MonoCarboxylate Transporter 1 ("MCT1") (used to increase lactate (necessary for all main aspects of carcinogenesis) transport outside of the cell)
3) Pyruvate Kinase M2 ("PKM2") (Glycolytic enzyme crucial for Warburg Effect glycolysis)
4) HexoKinase-2 ("HK2") (Glycolytic enzyme crucial for Warburg Effect glycolysis)

Theralase’s CLT was shown to downregulate glycolysis-related genes by approximately 20%.

In addition, Theralase’s CLT was shown to downregulate known oncogenes (genes that promote cancer progression) such as:

1) c-Myc ("master regulator" which controls many aspects of both cellular growth and cellular metabolism)
2) HIF-1α (responsible for cellular and developmental response during hypoxia)
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3) mTOR (a key metabolic and bioenergetic checkpoint which positively regulates protein, lipid and nucleotide synthesis)

Theralase’s CLT was also shown to increase the expression of known tumor suppressor genes (genes that inhibit cancer progression and are normally inhibited in cancer cells) such as p53, which regulate cell metabolism by lowering the rates of glycolysis and augmenting mitochondrial respiration. p53 downregulates cellular glucose uptake and the expression of other glycolytic enzymes.

Theralase’s CLT was shown to decrease oncogene expression by approximately 20% and increase tumor suppressor expression by 15%.

To evaluate the effect of Theralase’s CLT in an in vivo animal model, mice were injected with colorectal cancer cells (CT.26WT) and treated with Theralase’s CLT.

It was observed that Theralase CLT treated mice were able to survive on average twice as long versus untreated mice, due to a significant growth delay in tumour size caused by the anti-cancer effect of Theralase’s CLT (reversing the Warburg Effect).

Survival analysis after tumor injection:
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Based on the reported data, Theralase researchers have established, in a preclinical model, that Theralase CLT is able to:

1) Reverse the Warburg Effect (Decrease glycolysis (measured by reduced lactate production and increased mitochondrial respiration)); thereby, shifting the metabolic state towards normal cell energy production and away from cancer cell energy production
2) Downregulate the genes associated with the Warburg Effect
3) Downregulate oncogenes
4) Increase the expression of tumor suppressor genes
5) Significantly delay tumour growth

Thus, significantly increasing the overall survival rate of animals, exposed to cancer, who have been treated with Theralase’s CLT.

Mark Roufaiel, Ph.D., Research Scientist, Theralase stated, “A majority of cancer cells produce energy through a high rate of glycolysis and lactic acid production, a phenomenon known as the Warburg Effect. Our preclinical results clearly demonstrate that Theralase’s CLT is able to reverse the Warburg Effect and hence delay tumour progression. This new data changes the previous belief that CLT has carcinogenic effects and that CLT should not be used to treat cancerous tumours. In this latest research, we present preclinical evidence that Theralase’s CLT, in the proper clinical doses, is safe and effective in the reversal of the Warburg Effect and can modulate the cellular metabolism of cancer cells to selectively inhibit the Warburg Effect, in laboratory cancer models. This shows a significant untapped potential for Theralase’s CLT to be used as a safe, effective and elegant way to fight cancer.”

Arkady Mandel, MD, Ph.D., D.Sc., Chief Scientific Officer, Theralase stated that, “In our preclinical research, we employed knowledge garnered from exercise physiology in the treatment of patients suffering from muscular fatigue and pain, conditions that increase lactate production. Increased glucose uptake and the accumulation of lactate, even under normoxic conditions (aerobic glycolysis or the Warburg Effect), is a common feature of cancer cells. After a hiatus of several decades, there is a renewed interest in reversing aerobic glycolysis (Warburg Effect) as a key strategy to destroying cancer.”

Dr. Mandel went on to say that, “There are five key cellular indicators of the Warburg Effect in carcinogenesis (the formation of cancer):

1) increased glucose uptake
2) increased glycolytic enzyme expression and activity
3) decreased mitochondrial respiration
4) increased lactate production, accumulation and release
5) upregulation of genes, such as monocarboxylate transporters MTC1 and MCT4, for lactate exchange.

Lactate is the key metabolic compound involved in the above processes leading up to carcinogenesis; specifically: angiogenesis (development of new blood vessels), immune escape, cell migration, metastasis (cancer spread to other tissues) and self-sufficient metabolism. Accordingly, we strongly believe that technologies, like Theralase CLT, which have been proven preclinically to reverse the Warburg Effect, should be prioritized by researchers for the discovery of next generation anti-cancer therapeutic strategies. In our preclinical research, we used Theralase CLT as a modulator of cellular metabolism and were able to identify specific parameters that reverse the Warburg Effect, in laboratory cancer models. The results of our preclinical research demonstrate a significant unrealized potential of CLT, a therapeutic modality with over 50 years of clinical history that has been well recognized by Health Canada and the FDA as a safe and effective treatment of patients with chronic pain, now being able to
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provide an elegant way to fight cancer. Theralase, by building on the technology that commenced their early success in pain management, has now demonstrated the ability to employ this technology as a disruptive innovation in the destruction of cancer.”

Roger Dumoulin-White, P.Eng., President and CEO, Theralase stated, “The combination of technologies from our Therapeutic Laser Therapy (“TLT”) division and our Photo Dynamic Therapy (“PDT”) division is a pleasant surprise. Preclinical and clinical research have always been the drivers of innovation within our organization and the data strongly supports the use of Theralase CLT, according to very specific clinical dose specifications derived by Theralase, to be used pre-emptively to lessen the ability of cancer cells to defend themselves against PDT and the immune system, by reversing the Warburg Effect.”

About Theralase Technologies Inc.
Theralase Technologies Inc. (“Theralase®” or the “Company”) (TSXV: TLT) (OTCQX: TLFF) in its Therapeutic Laser Technology (“TLT”) Division designs, manufactures, markets and distributes patented super-pulsed laser technology indicated for the treatment of chronic knee pain, and in off-label use, the elimination of pain, reduction of inflammation and dramatic acceleration of tissue healing for numerous nerve, muscle and joint conditions. Theralase’s Photo Dynamic Therapy (“PDT”) Division researches and develops specially designed molecules called Photo Dynamic Compounds (“PDCs”), which have demonstrated an ability to localize to cancer cells and then when laser light activated, effectively destroy them.

Additional information is available at www.theralase.com and www.sedar.com.

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