LEMUTEPORFIN INJECTABLE FOR BENIGN PROSTATIC HYPERPLASIA

MARKETING PLAN FOR QLT INC.

By

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ABSTRACT

This paper is a marketing plan for QLT Inc. for its third-generation photodynamic therapy drug, Lemuteporfin. The paper focuses specifically on marketing Lemuteporfin as a new, *non-thermal* minimally invasive therapy for benign prostatic hyperplasia. The paper provides an insight into the external environment, or the competitive marketplace, and establishes the rationale for entering this marketplace. With this rationale, the internal environment, or the opportunity for Lemuteporfin within QLT, is analyzed and the strategic opportunities and challenges are introduced, along with a tactical plan to address the implementation of the strategies for Lemuteporfin related to penetrating and growing the minimally invasive therapy market in benign prostatic hyperplasia.

DEDICATION

To my dogs, Blarney and Paisley, that waited patiently for their walks while I was studying! To the Quinn family for their encouragement; to the Jovic family for their strength and love; to my husband, Steve, for his love and support, and to my son, Jack, for his unconditional love.

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Heartfelt thanks goes to Lee Anne Pilson. *Thank you, Lee Anne, for sending me on the road to achieving more.*

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GLOSSARY

AUASI	American Urological Association Symptom Index
BPH	Benign Prostatic Hyperplasia
CSF	Critical Success Factors
CME	Continuing Medical Education
CMS	Center for Medicare and Medicaid Services
FDA	Food and Drug Administration (U.S.)
HMOs	Health Maintenance Organizations
ILC	Interstitial Laser Coagulation
IPSS	International Prostatic Symptom Score
LUTS	Lower Urinary Tract Symptoms
MCOs	Managed Care Organizations
MIT	Minimally Invasive Therapies
NIDDK	National Institutes of Diabetes & Digestive & Kidney Diseases
NIH	National Institute of Health
NKUDIC	National Kidney and Urologic Diseases Information Clearinghouse
PDT	Photodynamic Therapy
PPOs	Preferred Provider Organizations
TUMT	Transurethral Microwave Thermotherapy
TUNA®	Transurethral Needle Ablation
TURP	Transurethral Resection of the Prostate
USD	United States Dollars

1 INTRODUCTION

1.1 Objective and Scope

The purpose of this paper is to construct a high-level strategic and tactical marketing plan for QLT Inc. for its product in clinical development, Lemuteporfin therapy, a new, *non-thermal* modality within the minimally invasive therapy class, in benign prostatic hyperplasia. The objectives are to communicate the important strategic considerations from both a market and product perspective, as well as to outline the important tactics for Lemuteporfin therapy to compete effectively in the minimally invasive therapy marketplace.

Chapter one provides a background on benign prostatic hyperplasia and an overview of the market for the current treatments of this disease, which include minimally invasive therapies. The chapter also defines the market trends that will contribute to the increase in the number of men with of benign prostatic hyperplasia, and the growth of the minimally invasive therapies market within this disease.

Chapter two provides an insight into the product concept for Lemuteporfin therapy and an analysis of the product opportunity within QLT from the perspective of the product's strengths, weaknesses, opportunities and threats and its strategic fit within the company.

Chapter three outlines the strategic considerations for Lemuteporfin therapy defining the approach the product will take to enter the minimally invasive therapy marketplace and the product positioning to compete effectively against alternative *thermal* minimally invasive therapies. Chapter four considers the high-level tactical steps for Lemuteporfin therapy,

addressing the most important issues for the product and the market. The tactics described take place prior to and following the launch of Lemuteporfin therapy.

1.2 Methodology

Data for this marketing plan were collected from both primary and secondary information sources related to the market for benign prostatic hyperplasia. The marketing plan reviews historical data from 2002 to assess the size of the market of current treatments for benign prostatic hyperplasia from the perspective of sales, prescriptions and number of procedures.

1.3 Background

QLT Inc. is a biopharmaceutical company located in Vancouver, British Columbia. The company is a world leader in the field of photodynamic therapy (PDT), the development of light-activated drugs to treat diseases. With this technology platform, and the assistance of commercial partners, QLT has commercialized two light-activated products, the first-generation PDT product, Photofrin® for the treatment of Barrett's Esophagus and lung cancer, and its second-generation PDT product, Visudyne® for the treatment of age-related macular degeneration. Today, the sole commercial PDT drug in QLT's portfolio is Visudyne®. This PDT product is the most significant commercial product for QLT and represents one of the most successful ophthalmic launches in pharmaceutical history.

Lemuteporfin is QLT's third-generation photosensitizer and is being developed for application in benign prostatic hyperplasia and dermatological conditions. With QLT's core competence in developing and commercializing PDT products, the company hopes to follow in the success of its first two PDT products and commercialize Lemuteporfin for benign prostatic hyperplasia. With its internal technical capabilities and commercialization experience with PDT drugs, QLT is committed to the success of its third-generation PDT drug, Lemuteporfin.

2 BPH SITUATIONAL ANALYSIS

2.1 Disease Overview

Benign Prostatic Hyperplasia (BPH) is considered a disease of aging that affects men into their 40s and beyond. It is an enlargement of the prostate due to the non-cancerous hypertrophy, or growth of tissue (epithelial, or inner tissue, and stromal, or outer tissue) within the prostate. The prostatic enlargement that can occur with BPH is the major cause of lower urinary tract symptoms (LUTS) associated with urinary voiding dysfunction from the bladder down the urethra (American Urological Association, Inc., 2003)[1].

There are two types of BPH: static or dynamic component (George Washington University, 2004). In static BPH the prostate enlarges due to the hyperplasia of epithelial tissue. With this prostatic enlargement, the prostate encroaches on the prostatic urethra causing the channel in the urethra to narrow making voiding from the bladder difficult. The symptoms of static BPH are considered obstructive and include hesitancy, weak stream, straining, dribbling, urinary retention, and incomplete emptying of the bladder.

In dynamic BPH, hyperplasia of the stromal smooth muscle of the prostate capsule occurs, not necessarily increasing the size of the prostate as in static BPH, but increasing smooth muscle contractions at the neck of the bladder outlet. These smooth muscle contractions lead to a sensation of urgency to urinate and cause a group of 'irritative' symptoms such as frequent, excessive urination during the night, painful or difficult urination, and burning.

[1] *With kind permission from the American Urological Association, Inc.*

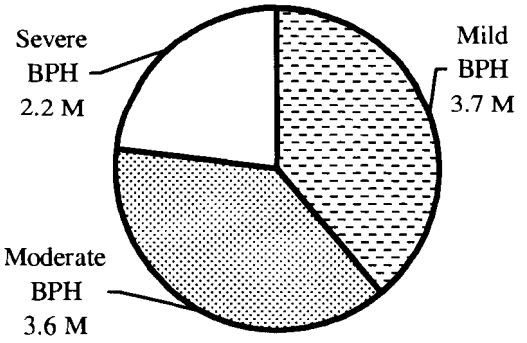
Benign Prostatic Hyperplasia can be classified as mild, moderate or severe BPH according to the American Urological Association Symptom Index (AUASI) questionnaire (Appendix 1) or internationally known as the International Prostatic Symptom Score (IPSS), that the patient is required to complete (American Urological Association, Inc., 2003). Mild, moderate and severe BPH is diagnosed based on both subjective (degree of obstructive and irritative bothersome symptoms as evaluated by the AUASI) and objective measures (urine flow, post voiding volume, ultrasound imaging to determine prostate size).

If BPH symptoms progress, serious complications can occur such as acute urinary retention which may lead to urinary tract infections and bladder inflammation (cystitis) (George Washington University, 2004). Long-term, complications such as kidney dysfunction and blood in the urine may present if the patient does not seek medical intervention. Most patients in the U.S. with bothersome BPH symptoms visit their physician before these complications. The goal of BPH treatments is to relieve symptoms and improve quality of life.

2.2 Prevalence and Incidence of Benign Prostatic Hyperplasia

In the United States, all men with clinically diagnosed BPH are categorized by severity of symptoms: 39% have mild BPH, 38% have moderate BPH, and 23% have severe BPH (Chestnut Partnership, 2002). In the U.S., approximately 90% of men in their 70s and 80s are symptomatic for BPH (National Kidney and Urologic Diseases Information Clearinghouse, 2004). With approximately 10.5 million males over the age of 70 in the U.S. (U.S. Census Bureau, 2004) and 90% of them with BPH, the breakdown by severity of symptoms is illustrated in Figure 1.

Figure 1 BPH Prevalence (2004)



Data source (BPH Prevalence Share by Severity): Chestnut Partnership, 2002, Report for QLT Inc.

Based on data (Prevalence) interpreted from the National Kidney and Urologic Diseases Information Clearinghouse, 2004; U.S. Census, 2004.

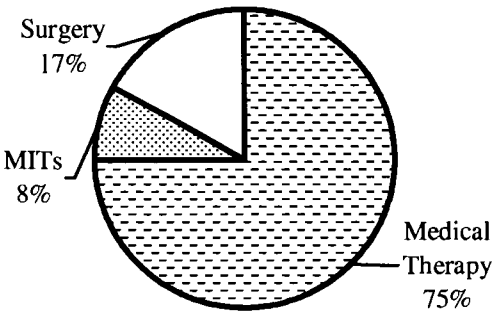
In 2000, in the U.S., there were approximately 4.5 million visits to a physician for BPH (National Kidney and Urologic Diseases Information Clearinghouse, or NKUDIC, 2004). The types of treatments for males symptomatic for BPH consist of medical therapy, minimally invasive therapy, or surgery. In the U.S., the number of males undergoing treatment is expected to grow with the introduction of uro-selective medical therapy, with less side-effects and improved minimally invasive treatment options for patients (Integrated Marketing Associates, 2001) (Chestnut Partnership, 2002).

2.3 Treatment Practice

A patient who is symptomatic for BPH will generally visit his primary care physician or general practitioner first. If the symptoms of BPH progress after watchful waiting (no drug or interventional therapy) or attempting drug therapy, the patient will usually be referred to a specialist called a urologist for further treatment. The urologist specializes in interventional therapy for BPH that includes minimally invasive therapies (MITs) and surgery. Figure 2

illustrates the relative share of each treatment used by urologists in practice (Chestnut Partnership, 2002).

Figure 2 BPH Treatment Share (2002)



Data source: Chestnut Partnership, Report for QLT Inc., 2002.

2.3.1 Medical Therapy

The two main classes of drug used for treating BPH are alpha blockers and 5-alpha reductase inhibitors. These can be used as either a monotherapy or a combination drug therapy. Both drug classes are effective in relieving the lower urinary tract symptoms associated with BPH via two different mechanisms that either addresses the static or dynamic components of the disease (George Washington University, 2004).

Alpha blockers relieve dynamic BPH symptoms by relaxing the smooth muscle contractions in the bladder neck and prostate gland to improve urine flow and reduce symptoms of urgency and frequency. Based on their mechanism of action, alpha blockers are considered the best medical therapy option for BPH because they provide immediate symptom relief (George Washington University, 2004). However, they require the patient to take a pill once-a-day and are associated with side-effects such as dizziness, low blood pressure and intestinal problems (American Urological Association, Inc., 2003).

The older alpha blockers (Hytrin®, Cardura® and generics) were initially indicated for cardiovascular conditions such as hypertension when it was noticed that, secondary to treating this, these drugs increased urine flow in males with lower urinary tract symptoms. Due to the side-effects of hypotension (i.e. dizziness) in individuals without high blood pressure, newer alpha blockers were developed which are considered to be uro-selective (Flomax® and UroXalatrol®), thereby reducing the incidence of hypotensive side-effects.

5-alpha reductase inhibitors decrease the prostate size, working on the static component of BPH. There are two approved drugs, Proscar® and Avodart™, in this class of drug and their mechanism of action is such that symptom relief in the BPH patient is usually felt within the first three months of taking the drug (George Washington University, 2004). Daily dosing of the drug is required. Side effects associated with this class of drug may include a low incidence of sexually related dysfunctions (George Washington University, 2004).

Based on a panel of urologists formed by the American Urological Association to assess current treatments for BPH, the conclusions drawn were that alpha blockers achieved on average a 6 to 8 point drop in AUASI scores and 5-alpha reductase inhibitors achieved on average a 3 to 4 point drop in AUASI scores (American Urological Association, Inc., 2003). Therefore, drug therapy was found to contribute to a modest to moderate improvement in a patient's BPH condition. However, 30 to 40% of men discontinue use of medical therapy within one year due to limited efficacy, side-effects and compliance (George Washington University, 2004). Additionally, the long-term cost of medical therapy (i.e. men may continue years of medical therapy treatment) prompt more men to choose an alternative "one-time" intervention for BPH by undergoing a procedure from the class of therapies known as minimally invasive therapies (Integrated Marketing Associates, 2001).

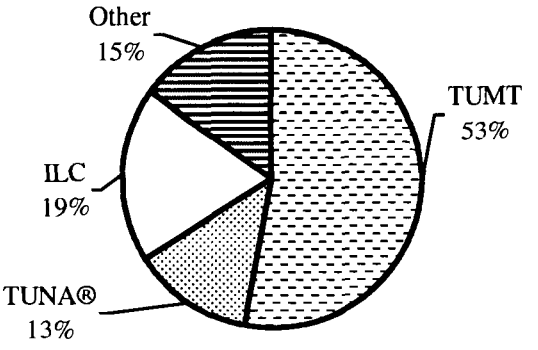
One area of drug therapy that is gaining interest is the use of a combination therapy of an alpha blocker and 5-alpha reductase. In a National Institute of Diabetes and Digestive and Kidney Diseases clinical study (Medical Therapy of Prostatic Symptoms), combination therapy was shown to delay the progression of BPH out to 5 years which is better than either drug used alone (National Kidney and Urologic Diseases Information Clearinghouse, or NKUDIC, 2004). However, combination therapy may also increase the number of side-effects compared to either drug used alone and is only suitable for select patients with BPH.

2.3.2 Minimally Invasive Therapies[2]

Minimally invasive therapies are a procedural-based class of therapies for BPH that are mainly performed in a urologist's office and therefore considered *office-based.* Current MITs employ *thermotherapy* using microwave, radio frequency, laser, hot water, or ultrasound energy to heat the prostate tissue to temperatures ranging from 45^0C to 50^0C which causes irreversible tissue necrosis in the prostate. Approved MITs on the market, such as the most widely used therapies of Transurethral Microwave Thermotherapy (TUMT), Transurethral Needle Ablation (TUNA®) and Interstitial Laser Coagulation (ILC), de-bulk prostatic tissue and relieve obstruction to improve urine flow. Other MITs not widely used include water-induced thermotherapy and high-intensity ultrasound destruction of prostatic tissue. Figure 3 illustrates the relative market share of approved MITs on the market (Chestnut Partnership, 2002).

[2] *Description of MITs (patient type, procedure, treatment effect, catheterization and side-effects) compiled from QLT primary market research from past several years, unless otherwise referenced.*

Figure 3 Treatment Share by Type of MIT (2002 U.S. Data)



Data source: Chestnut Partnership, Report for QLT Inc., 2002.

The panel of urologists who reviewed the American Urology Association guidelines in 2003 concluded that all thermal-MITs approved for use in the market achieved a moderate to large improvement in symptoms, or a 9 to 11-point improvement in AUASI scores (American Urological Association, Inc., 2003). However, MITs were associated with side-effects such as pain during the procedure, bleeding, urgency and frequency, and urinary tract infections in men, and in the case of a certain type of MIT procedure (Transurethral Needle Ablation), may only be effective in 70% of men who undergo treatment (George Washington University, 2004). As a result, weighing the benefits/risks associated with MITs, generally the patient population most likely to undergo a MIT procedure is one where their BPH symptoms are considered moderate to severe.

2.3.2.1 Transurethral Microwave Thermotherapy

Transurethral Microwave Thermotherapy (TUMT), with approximately a 53% share of the MIT market (Figure 3), is the most popular BPH therapy procedure used in a urologist's office. The first TUMT device was approved in 1996 and today there are several device manufacturers.

A TUMT procedure is best performed on prostate sizes that are small to medium in size. The procedure is a 2-step process requiring the insertion of an anchoring balloon and a microwave antenna via a catheter through the urethra and a temperature probe inserted through the rectum. The balloon catheter is used to ensure correct positioning and non-migration of the microwave antenna during the procedure. Prior to the introduction of the balloon catheter in 2000, there were several reports of serious adverse events that involved significant tissue damage to the penis and urethra.

When the microwave antenna is turned on, cool water circulates through the catheter, preventing any damage to the prostatic urethra while the rectal probe measures the temperature of surrounding tissue outside the prostate protecting against any peripheral damage. Typically, local anesthesia and conscious sedation is given prior to treatment to minimize the discomfort associated with TUMT. The procedure can be performed in a urologist's office and takes about 30-60 minutes to perform with an additional 30-45 minutes of pre- and post-treatment preparation. Following the procedure the patient is usually catheterized up to one week depending on the temperature used to de-bulk prostatic tissue allowing for ease of voiding. Improvements in urine flow and BPH symptoms usually take place between 6 to 12 weeks following tissue swelling and healing.

Side-effects associated with the TUMT procedure may include intra and post-procedural pain, blood in urine, irritation and an inability to urinate after the procedure due to swelling. In some cases, concomitant use of alpha blockers for a period of 3 months is prescribed to help alleviate the urinary dysfunction associated with tissue swelling of the prostate. Urinary retention and urinary tract infections may also be associated with the procedure. Additionally, the procedure may not be effective in up to 30% of men and as much as 25% of men can experience loss of ejaculate when a lower temperature, or cooled thermotherapy, is used to minimize pain during the procedure (George Washington University, 2004).

The latest TUMT device to be approved by the FDA in the U.S. in February 2004 is the Prolieve™ System manufactured by Celsion and marketed by Boston Scientific. This TUMT device is marketing the added advantage over alternative TUMT devices of thermodilation whereby the balloon catheter in the prostatic urethra provides increased dilation in the urethral channel, acting as a natural stent during the 45 minute procedure (Celsion, 2004). Celsion/Boston Scientific claim that their TUMT device requires no sedation during the procedure and generally no post-procedural catheterization.

2.3.2.2 Transurethral Needle Ablation

Transurethral Needle Ablation (TUNA®) can be performed on prostates ranging from sizes of medium to large and with men who have a prostatic median lobe (prostatic tissue surrounding the bladder neck transversely compared to the lateral lobes of the majority of prostates). Similar to TUMT, TUNA® employs heat via radiofrequency energy to de-bulk prostatic tissue to improve urine flow. Currently, there is only one TUNA® device on the market: the Precision TUNA® manufactured and marketed by Medtronic.

With a TUNA® procedure, the probe is inserted through the urethra and deployed into the prostate via a small puncture wound. The probe contains two electrodes that transmit radiofrequency waves between each other to cause concentrated areas of necrosis. The entire procedure is performed under urologist's visualization via a cystoscope to enable the urologist to be selective in choosing the areas of necrosis. Local anesthesia is generally given prior to a patient undergoing a TUNA® procedure. The entire procedure can be performed in the urologist's office or in an outpatient setting in 45-60 minutes with approximately 30-45 minutes of pre- and post-treatment preparation. Catheterization after the procedure usually lasts between 3 to 5 days, with approximately only 40% of patients requiring this, according to Medtronic (Medtronic, 2005). Time to improvement for urine flow and BPH symptoms depends on the area

of necrosis and prostate size, however may typically take place anywhere from 2-6 weeks. Side effects associated with the TUNA® procedure may include bleeding, discomfort, and urgency and/or urinary tract infections in men undergoing the procedure.

2.3.2.3 Interstitial Laser Coagulation

Interstitial Laser Coagulation (ILC) was recently approved for use in an office-based setting, moving this procedure from being solely offered in an outpatient setting. ILC uses focused laser energy to create heat and areas of necrosis in prostatic tissue to improve urine flow in BPH patients. The only approved device on the market for ILC is offered by Johnson & Johnson and is marketed as the Indigo® Laser Treatment System.

An ILC procedure can be performed on prostates ranging from medium to large in size. ILC is conducted under the urologist's visualization via a cystoscope. The fiber optic is inserted into the prostatic tissue and the laser is turned on to generate heat and precisely target the enlarged areas of the prostate to relieve obstruction. A prostatic block and local anesthesia are given to minimize patient discomfort during the procedure. The procedure time can range from 30-60 minutes depending on the size of the prostate, with approximately 30-45 minutes of pre- and post-treatment preparation. Following the procedure, patients may be catheterized up to one week. Symptom improvement usually begins within 3 to 4 weeks following the procedure. Similar side-effects to those of TUMT and TUNA® may be experienced by men undergoing the procedure.

2.3.3 Transurethral Resection of the Prostate[3]

Transurethral Resection of the Prostate (TURP) is a surgical procedure that has been used since the 1950's and it is performed in a hospital setting, or, in some cases, in an ambulatory outpatient setting. Procedure volumes associated with TURP have decreased significantly over the last 10 to 15 years as there has been greater pressure to reduce hospitalization costs in favour of using minimally invasive treatments such as TUMT, TUNA® and ILC that can be performed in an office-based setting, thereby reducing overall procedural costs to the healthcare system.

Generally men with large prostates, severe BPH symptoms, or those who have progressed to the point of urinary retention are candidates for TURP. TURP is the endoscopic removal of a portion of the prostate using electrodes in the form of a resectoscope that coagulate and remove tissue via suction. It is performed under general anesthesia and usually takes approximately 45 to 60 minutes for the procedure alone, depending on the size of the prostate. Following the procedure, patients are usually kept in the hospital from one to three days. However, as mentioned in the preceding paragraph, there is a growing trend to release these patients within 24 hours to reduce hospitalization costs. Typically patients are catheterized for up to 2 weeks depending on the post-procedural swelling and irritation.

With TURP, improvements in symptoms can occur as early as three weeks after the procedure. TURP is considered the "gold standard" of treatments for BPH as it achieves significant (90%) improvement in BPH symptoms and urine flow, better than any alternative treatment (George Washington University, 2004). However, along with these improvements, complication of bleeding and infection is higher with TURP compared with alternative treatments for BPH.

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[3] *Description of invasive procedures (trends, procedure, treatment effect, catheterization and side-effects) compiled from QLT primary market research from past several years, unless otherwise referenced.*

2.4 Pricing of BPH Treatments[4]

Medical therapy for BPH can range anywhere from USD $500 to $1,000 per year depending on whether a generic or branded product is prescribed to a BPH patient. The length of time a BPH patient remains on medical therapy can vary due to patient's preference, incidence of side-effects or effectiveness of medical therapy to relieve symptoms, and can range anywhere from one to several years (Integrated Marketing Associates, 2001).

Minimally invasive therapies have a disposable and a capital device component associated with the procedure. The disposable component has an average cost of USD $1,000 per unit whereas the capital device component initially was priced between USD $50,000 and $100,000 when these MIT devices were first introduced, however, today, these devices have been reduced in price and approximately sell in the price range of USD $25,000 to $40,000. Additionally, there is a procedural cost with MITs that come from the urologist's time to perform the procedure. This can range anywhere from $2,500 to $4,000 depending on the state where the procedure is performed.

TURP uses relatively low-cost disposable electrodes compared to medical therapy and MITs, however the hospital costs associated with the procedure can range from USD $8,000 to $12,000 depending on the state where the procedure is performed in.

2.5 Summary of Current BPH Treatments in the U.S.

Table 1 provides a list of the BPH treatments described in the previous sections including a summary of the patient populations they are suitable for, their associated benefits and risks, and cost of treatment.

[4] *Information on pricing compiled from QLT primary market research from past several years.*

Table 1 Summary of Current BPH Treatments in the U.S.

Class	Patient Population	Efficacy (average decrease in AUASI)	Advantages or Benefits	Disadvantages or Risks	Cost
Medical Therapy	Moderate to severe BPH	30%	• Prescription medication	• Patient compliance • Hypotension and sexual side-effects	Up to $1,000 per year
MITs	Moderate to severe BPH	50%	• Possibly a one-time treatment • Office-based with patient under local anesthesia	• Pain during procedure • Requires catheterization • Bleeding, urinary retention, and abnormal ejaculate	Up to $4,000 for a procedure
Invasive Procedures	Moderate to Severe BPH, Patients with acute urinary retention	80-90%	• High possibility of a one-time treatment • Most effective BPH treatment	• Requires catheterization • High incidence of bleeding and retrograde ejaculation • Requires high level of physician skill • Out-patient or in-patient procedure (i.e. not office-based)	Between $8,000 to $12,000 per procedure

2.6 Drivers for BPH Treatment Growth

2.6.1 Demographics

In the U.S., the increasing median age of the population will be driven by the baby boom population. According to the U.S. Census Bureau, by 2011, this group will have its first members reach the age of 65 and will represent 25% of the total population in the U.S., or approximately 75 M residents compared to 35 M residents in 2000 (or 12% of the total population in 2000) (U.S. Census Bureau, 2004). As mentioned in Section 2.2, 90% of males in their 70s and 80s are

symptomatic for BPH. As a result of the aging population growing, more and more men will be diagnosed with BPH and require some medical attention for their disease.

2.6.2 Reimbursement

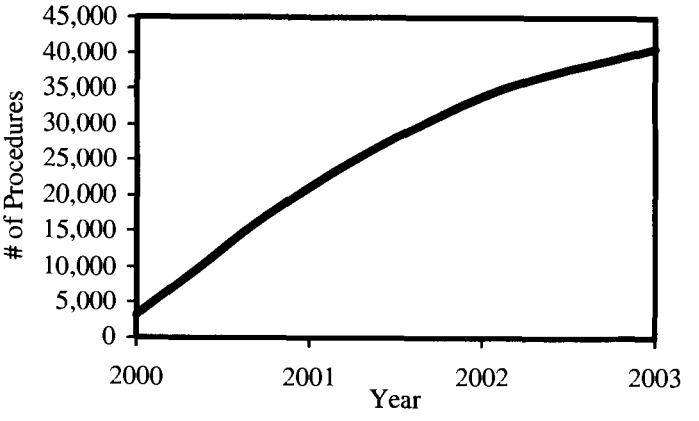
In the U.S., approximately 70% of males with BPH are medically insured by Medicare (Surveillance Data Inc., 2003), the government-funded healthcare plan for individuals over the age of 65. Under Medicare, medically necessary procedures are covered after a deductible is paid, and in 2006 prescription drugs will be covered as well to a limit. The agency responsible for implementing and mandating Medicare policies is the Center for Medicare and Medicaid Services (CMS).

Reimbursement dynamics in the U.S. for BPH were revised to promote the use of office-based therapies for BPH, such as MITs, for appropriate patient types in an effort to reduce the hospitalization costs associated with invasive procedures such as TURP (average cost to Medicare is $8,000 to $12,000 per procedure as mentioned in Section 2.4). Prior to 2002, reimbursement to the urologist for performing a MIT procedure was sub-optimal as the devices used to perform the procedures when they were first marketed in the late 1990's and early 2000's, targeted the hospital market, therefore a greater portion of the reimbursement to urologists for performing MIT procedures was used to cover associated hospital costs. However, as device companies began targeting office-based urologists, reimbursement guidelines were revised by CMS to reflect a procedural code for MIT use in the office thereby increasing reimbursement to the urologist for performing a MIT procedure compared to performing a TURP procedure, as this procedural setting for a MIT spared any expensive hospitalization costs.[5] As a result, MIT

[5] *Information on reimbursement trends compiled from QLT primary market research from past several years.*

procedures have experienced significant growth (Figure 4) compared to a decline in TURP procedures (Chestnut Partnership, 2002).

Figure 4 MIT Volume of Procedures in the U.S.



Data source: Surveillance Data Inc., Report for QLT Inc., 2004.

3 OPPORTUNITY ANALYSIS FOR QLT

3.1 Photodynamic Therapy with Lemuteporfin for BPH

Based on feedback from both qualitative and quantitative market research with investigators from QLT's phase I/II trial, practicing urologists, and patients a product concept exists that has been tested to determine product adoption and characteristics that will contribute to demand for Lemuteporfin in BPH. Today, the concept reads as follows:

> Photodynamic therapy with Lemuteporfin (PDT) is an office-based minimally invasive procedure for symptomatic BPH, and unlike thermal MIT procedures, uses non-thermal light to activate the photosensitizer that is injected in the prostate.
>
> Following the application of a local anesthetic, the urologist will insert a cystoscope, and through the cystoscope an injection system is inserted to deliver a set dose of Lemuteporfin into the prostate. Following removal of the injection system, an anchoring balloon is inserted into the bladder to ensure proper positioning of the fiber optic along the prostatic urethra. After a 15 to 30 minute waiting period, the urologist or assistant turns on the laser unit for a period of five minutes that allows the fiber optic to deliver light to the prostate to activate Lemuteporfin.
>
> Minimal bleeding and irritation may occur during the procedure, however the patient requires no catheterization and relief of BPH symptoms, similar to current MITs, should occur within 4 weeks.

3.2 Unmet Need in Minimally Invasive Therapies for BPH

Urologists interviewed in a qualitative market research study and the urology investigators in QLT's Phase I/II study pointed out that there were several unmet needs with current minimally invasive therapies on the market. Those MITs considered effective also

produce significant irritation to the patient and prolong the time to relief of BPH symptoms making patient acceptability a challenge. Conversely, those MIT procedures that have greater patient acceptability usually result in marginal efficacious benefit over medical therapy. As a result, there is a place for Lemuteporfin therapy in BPH if it demonstrates a significant efficacious benefit over medical therapy with a good patient acceptability profile compared to alternative MITs.

Additionally, a therapy that is safer due to a reduced risk of the urologist causing peripheral damage outside the prostate fulfils an unmet need with minimally invasive therapies as these current *thermal* therapies require temperature monitoring to ensure safeguards and prevention of necrosing surrounding tissue of the prostate. Lemuteporfin therapy can deliver on this need as a tissue necrosing effect is only delivered if the drug and the light components of the therapy interact, therefore an injection of the drug into tissue outside the prostate will not cause necrosis as the fiber optic only shines light on the prostate due to reflective shielding that acts as a safeguard for the fiber optic preventing light from penetrating into the bladder or below the level of the prostatic urethra.

3.3 Value to End-users

3.3.1 Physicians

Lemuteporfin therapy as an office-based procedure will only be successful with urologists if it offers the equitable, or better, reimbursement and treats the same broad base of *symptomatic* BPH patients as the other minimally invasive therapies. In addition, economic value received by urologists from performing Lemuteporfin therapy for BPH is possible if the barriers to use are minimal. These include offering flexible payment terms such as leasing or pay-per-use terms for the capital device component of the therapy and providing a packaged drug/device

disposable component to minimize reimbursement coding procedures (i.e. one product code vs. two product codes).

3.3.2 Patients

Patients will find value in undergoing a treatment with Lemuteporfin therapy if the data are similar or better to current MITs and allows patients to improve their quality of life, with reduced BPH symptoms, sooner than alternative MITs. Advantages to Lemuteporfin therapy valued by patients will be a greater chance of avoiding catheterization with this procedure vs. alternatives, a faster onset of action, and a simple, painless procedure that can be performed in their doctor's office.

3.3.3 Payors

Lemuteporfin therapy in BPH is an attractive option for payors if the therapy is able to deliver long-term results, with few incidences of retreatments, similar to current MITs on the market that have a relatively low incidence of retreatments. Based on data from the five-year follow-up for TUNA® and TUMT, the average retreatment rate is reported as up to 20% of patients requiring an alternative procedure for their BPH symptoms. Compared to medical therapy, Lemuteporfin therapy will need to have durable data extended between 4 and 5 years to demonstrate that this type of minimally invasive therapy can be cost-effective over long-term drug use. Long-term follow-up of patients in Phase II and III as well as a pharmacoeconomic analysis will establish a cost/benefit case for Lemuteporfin therapy compared to alternatives for payors.

3.4 Synergy with QLT Portfolio

Lemuteporfin represents QLT's third-generation PDT drug. The company's core technology has evolved from the development of PDT drugs, with its most successful product being Visudyne®, a PDT drug to treat age-related macular degeneration, the leading form of blindness in individuals over the age of 50. Core competences within QLT include scientific and commercial expertise to develop and commercialize PDT drugs. Access to highly skilled scientists in the field of photodynamic therapy is internal to QLT, and as a result, Lemuteporfin enjoys a high probability of developmental success. Technical know-how to developing PDT drugs is embedded within the organization thereby enabling QLT to efficiently progress PDT products along the clinical pathway. With these competences, and the financial backing QLT receives from its success with Visudyne, QLT is committed to the research and development of photodynamic therapy, allowing the company to expand on the therapeutic indications its drugs can treat.

Following the closing of the acquisition of Atrix Laboratories by QLT Inc. in November 2004, QLT's portfolio expanded to include Eligard®, a luteinizing release hormone agonist indicated for advanced prostate cancer. With Eligard®, QLT will have exposure selling to urologists and this exposure will help QLT in preparing to launch Lemuteporfin therapy for BPH, another urology product that will be used by the same target customer. There may be opportunities for efficiency and synergistic marketing/selling efforts with the availability of two urology-based products promoted by one sales team to one customer.

Lemuteporfin therapy represents an opportunity for QLT to exploit internal competences by combining the product (PDT drug) development expertise with the market know-how (Eligard® in urology). Addressing both product and market challenges with internal competences facilitates a plan for success when launching a biopharmaceutical product. With

these internal competences and the BPH minimally invasive market size that will transpire, Lemuteporfin therapy is a good fit for QLT and an opportunity that should continue to be pursued.

3.5 Lemuteporfin S.W.O.T. Analysis in BPH

Lemuteporfin therapy in BPH has the potential to do well in the U.S. if our data and usability compared to alternative MITs are competitive and reimbursement for our therapy is at least equitable to alternative MITs. The market for minimally invasive therapies is competitive; however the overall market is growing, therefore a well-positioned MIT will do well amongst alternatives. To understand the value of Lemuteporfin therapy within QLT, an analysis of its Strengths, Weaknesses, Opportunities and Threats is warranted. This analysis can be characterized by both the market and technical, or product, attributes of Lemuteporfin.

3.5.1 Strengths

The BPH market for Lemuteporfin is anticipated to grow significantly due to the aging baby boomers. In North America, access to healthcare is prominent and the treatment for diseases of age such as BPH, are prevalent. Specifically, the market for minimally invasive therapies, as Lemuteporfin therapy, will grow as the trend to treat diseases of age with office-based, one-time procedures that offer a safe and effective alternative to costly hospital-based procedures or chronic, expensive long-term use of medical therapy for BPH.

To highlight product strengths with Lemuteporfin therapy, data to date are promising indicating that Lemuteporfin performs as well as alternative MITs in the marketplace. Clinical data from the Phase I/II trials demonstrate that Lemuteporfin achieves an average reduction in AUASI scores similar to that of transurethral microwave thermotherapy. This finding coupled with the product features of Lemuteporfin injectable being locally delivered into the prostate and

the fact that it is a *non-thermal* light-based therapy for BPH performed in the office, contribute to the product strengths and make this therapy attractive to patients, urologists and payors.

3.5.2 Weaknesses

While the market for minimally invasive therapies is anticipated to grow, currently there are no historical data to demonstrate this. Data show that the grow rates of MITs are significant, however, the overall number of procedures is considered small and makes an investment into the development of Lemuteporfin questionable if the market were to remain at its current state. Therefore, the weakness lies in the inherent risk of relying on the MIT market to grow. However, trends for treating BPH all favour growth in this marketplace. Initiatives such as providing favourable reimbursement for office-based procedures to reduce hospitalization costs and patients electing for one-time non-invasive procedures for BPH compared to chronic medical therapy with side-effects or invasive procedures all support the rationale that the MIT market will grow.

Lemuteporfin will require urologists to buy into another MIT capital device. If the urologist already has a device in place for performing a TUMT or TUNA® procedure, acquiring another capital device represents a barrier to use for Lemuteporfin therapy, and therefore is considered a weakness of the product. Strategic options, as will be outlined in Section 4, demonstrate that this barrier to use can be overcome based on better product features compared to alternative MITs, and an understanding by QLT that the source of revenue for the company based on its current business model, is in the disposable drug/device market not the capital device placement market.

3.5.3 Opportunities

With implementation of effective marketing tactics, there is an opportunity to facilitate growth in the market for MITs by positioning Lemuteporfin therapy as a first-line treatment for

moderate to severe BPH. Focus on the referral networks and patients through education and direct-to-consumer campaigns will help to drive this market development strategy. Influencing the American Urological Association to establish Lemuteporfin therapy as a first-line treatment may be another option to grow the market. This strategy is somewhat risky as it can be viewed negatively by the urology community if one type of MIT treatment is focussed on in the treatment guidelines, however, this may be accomplished indirectly with payors. Pharmacoeconomic data comparing the increased benefit/cost ratio of Lemuteporfin compared to alternative treatments will influence payors to re-examine the armamentarium of BPH treatments and provide incentives to urologists to use a therapy, such as Lemuteporfin, that is cost-effective. With a greater number of urologists adopting Lemuteporfin and becoming well versed in its features and benefits, this group can influence AUA to revise the treatment guidelines.

From the product perspective, Lemuteporfin has an opportunity to gain greater patient and physician acceptance compared to alternative MITs. Lemuteporfin offers a therapy that is *non-thermal* and as a result there is little risk of damage to peripheral tissue outside the prostate compared to thermal therapies. Distinct features of the non-thermal Lemuteporfin therapy that offer greater patient acceptability include faster onset of action due to less irritation and swelling of the prostate, and a reduced need for catheterization. Physician acceptability is increased due to the ease of administrating a non-thermal therapy that requires no temperature monitoring with rectal probes thereby increasing safety and reducing the time of the procedure, and their patient satisfaction with an effective and *safer* therapy.

3.5.4 Threats

A threat to the market for minimally invasive therapies will be the entrant of a medical therapy with a new mechanism of action with improved efficacy over current medical therapy that will delay the progression of a patient moving from drugs to procedures. Another threat to

Lemuteporfin therapy competing in the MIT market will be the introduction of a new MIT that has a non-thermal approach and is able to achieve similar or better efficacy than current MITs. Both these threats together will slow MIT market growth and adversely affect the market share for Lemuteporfin therapy.

Receiving a reimbursement level lower than current MITs for Lemuteporfin therapy is a threat to the uptake of the product by urologists, as urologists will remain with a product that provides financial incentive to their practice if all else is equal (i.e. efficacy and safety). Additionally, as Lemuteporfin therapy will not have first-mover advantage into the MIT marketplace, the threat to product uptake remains with the fact that TUMT and TUNA® will have long-term clinical data of five years or more, and will have gained a comfort level with urologists, as well, these MITs will have an opportunity to evolve from their current form to potentially better versions of the same type of treatment.

4 MARKETING STRATEGY

4.1 Critical Success Factors

The critical success factors (CSF), listed below, need to take place in their entirety in order to successfully implement the marketing strategy for Lemuteporfin in benign prostatic hyperplasia.

1. **Developing Strong Opinion Leader Support** - Photodynamic therapy with Lemuteporfin is a new MIT modality for treating benign prostatic hyperplasia. Working with key opinion leaders early in development will be critical to building advocacy and developing a user base to which other physicians will look for guidance on the usage of Lemuteporfin therapy in BPH closer to the product launch.

2. **Controlling Distribution and Pricing of Disposables** - Photodynamic therapy with Lemuteporfin will need to be priced competitively with the disposables of alternative MIT therapies on the market. QLT taking responsibility for the ownership of the manufacturing and distribution of the drug and device disposables will assist in controlling the cost of goods and setting a margin that the company can regulate relative to the market price of alternative MIT disposables.

3. **Establishing Favourable Reimbursement** - Photodynamic therapy with Lemuteporfin will need to be at least equal to or better than the reimbursement received by urologists for performing alternative MITs. Factors influencing reimbursement will depend on the efficiency of the procedure (i.e. the payback the urologist receives relative to the investment of time and money he/she gives to perform the procedure), the use of the therapy for a broad base

of patients and the effectiveness of the procedure from a physician, patient, and payor perspective.

4. **Promotional Message Development Emphasizing Usability, Safety and Cost-Effectiveness of Lemuteporfin** - The data for Photodynamic therapy with Lemuteporfin in BPH thus far have demonstrated that the therapy achieves a range of a 40-60% drop in AUASI scores, similar to the performance of alternative MITs currently on the market. The success of Lemuteporfin in BPH will depend on factors of usability, rather than efficacy, which are marketable advantages over alternative MITs. These factors include a non-thermal approach to damaging prostate tissue, less time to perform the procedure in an office-based setting, less post-procedural irritation for the patient, and therefore fewer post-procedural catheterization events, and a faster onset of action to desired efficacy.

4.2 Market Opportunity Defined

Lemuteporfin therapy will follow a two-pronged market strategy. Initially, in the short-term following the launch of Lemuteporfin, the focus will be on market penetration into the existing minimally invasive therapy market to compete directly with thermal-based MITs. A longer-term approach will be extending the opportunity to present Lemuteporfin as a first-line therapy for BPH patients with moderate to severe symptoms.

4.2.1 Market Penetration Strategy

Lemuteporfin, once launched, will compete with thermal-based MITs for new BPH patients who will receive a procedural treatment for their symptoms at the urologist's office. In order for Lemuteporfin to succeed in undertaking this strategic plan, an aggressive promotion and distribution campaign will need to be implemented to effectively position the benefits of safety, efficacy and usability of this light-based therapy over thermal-based MITs, as well as ensure

maximum penetration of the capital equipment and product into urologists' offices. This campaign will focus on urologists primarily where the marketing and sales teams will communicate messages honing in on the economics of the therapy (reimbursement and usability) as well as the safety and efficacy urologists can deliver to their patients with Lemuteporfin therapy.

The market penetration strategy will rely on promotion momentum to gain maximum penetration into the minimally invasive therapy marketplace. QLT will need to invest financial resources significantly in creating awareness for Lemuteporfin therapy among urologists. Assistance from key thought leaders and clinical investigators to effectively present the clinical data at major urological forums, such as the American Urological Association meeting, will be critical to building a user base for the product.

4.2.2 Market Development Strategy

The longer-term market strategy for Lemuteporfin will be for QLT to position the therapy as a first-line therapy for patients with moderate to severe BPH. This approach will grow the market for minimally invasive therapies overall, increasing the market share for Lemuteporfin, rather than relying on cannibalizing the market share of alternative MITs. In following this market development strategy, QLT will need to focus on patients and referral networks such as general practitioners.

Targeting patients will require direct-to-consumer advertising to reach patients and allow for a "pull" strategy for the uptake of Lemuteporfin therapy where patients will go directly to their general practitioner or urologist and inquire about the features of the therapy. Developing this market will require both education and awareness of Lemuteporfin therapy. Before these tactics can take place, identifying which demographic to target is critical. As indicated in Section

2.2, 90% of men have BPH by the time they reach their 70s and 80s. Channels to reach patients will need to be applicable to the demographic associated with BPH.

With the target demographic of 70 to 80-year old men, education about Lemuteporfin therapy towards men can be accomplished through medical websites or through patient health brochures found at pharmacies. The rationale for selecting these channels is attributed to the assumption that the majority of this group is retired, potentially on concomitant medication for other conditions/diseases and therefore is adept at self-diagnosing oneself with the technology available today. Following education about Lemuteporfin therapy, direct-to-consumer advertising can appear in leisure journals, commercials on television programs and radio programs that target retirees.

Market development from the physician perspective will focus on the referral networks of urologists such as the general practitioner group. This group will need to be educated on the BPH patient type that is suitable to be referred to the urologist's office for a minimally invasive procedure. Successful accomplishment of educating general practitioners on the patient type will result in BPH patients being brought to treaters (urologists) of Lemuteporfin therapy more rapidly, thereby growing the market more quickly, than if this patient type were allowed to follow the current practice dynamic of treating these patients with medical therapy first in the care of general practitioners.

4.3 Customer Segmentation Strategy[6]

QLT will focus on three primary customers when marketing Lemuteporfin therapy for BPH: the physician, the payer, and the patient. In conjunction with marketing efforts targeting these groups, QLT will create awareness with referral networks such as general practitioners and

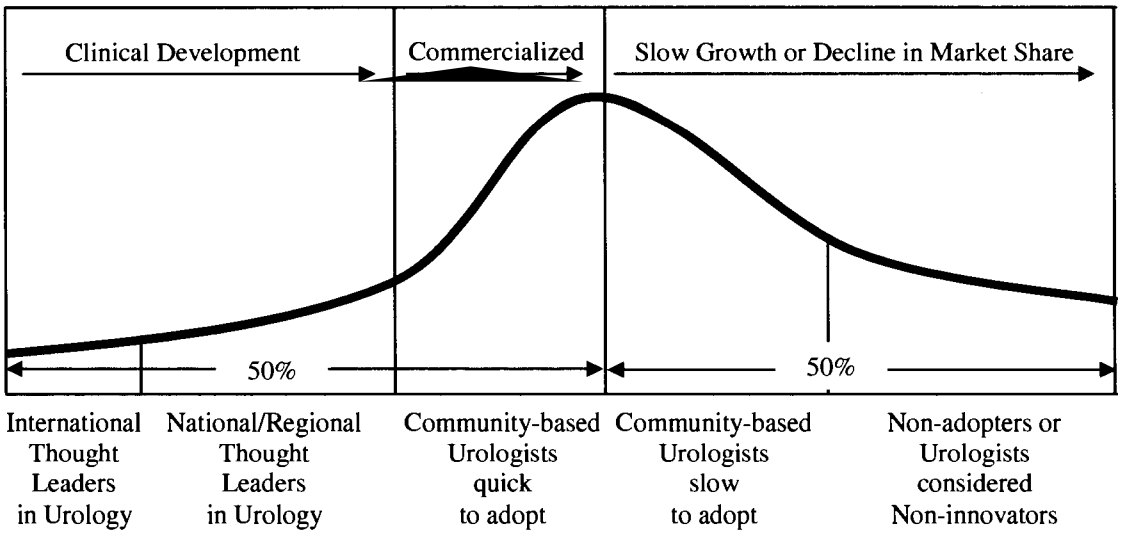
[6] *Strategy adapted from GEMS™ Business Plan, 2004, by permission.*

supportive care staff such as urology assistants to further drive interest and use for Lemuteporfin therapy.

4.3.1 Urologists

For the primary market segment of urologists, adoption of Lemuteporfin therapy will follow stepwise similar to Rogers', 1995, adoption diffusion curve. Rogers' identifies the market segments of the adoption diffusion curve from left to right as: Innovators, Early Adopters, Early Majority, Late Majority and Laggards. Figure 5 illustrates the market adoption of Lemuteporfin with the different segment of urologists applied to the adoption diffusion curve. Innovators or first-tier urology groups considered to be the thought leaders and national opinion leaders in urology will be identified early in development (Phase I/II clinical stage) as the product "gurus" that are willing to buy into an unproven concept. Early adopters or national and regional opinion leaders will also need to be identified during clinical development. Efforts to persuade these two adopter groups to be involved will include the promoting of Lemuteporfin therapy in BPH, clinical trial involvement and other advocacy activities such as membership on advisory groups or safety review committees.

Figure 5 Adoption of Lemuteporfin in Urology



Based on Rogers, E. M. (1995). Diffusion of Innovations. The Free Press, New York.

Following launch, major promotional programs such as personal selling, journal ads and presence at major conferences should be targeted to early majority and late majority, or community-based urologists, and preferably those adopters that are in group practice maximizing treatment volume based on a fewer number of capital laser units installed. In the U.S. approximately 400 large group practices and approximately 1,000 small group practices exist[7].

At the launch stage, Lemuteporfin therapy will need to be marketed as a simple procedure with a clear economic incentive for the urologist's practice. Urology management tools will need to be developed that will simplify reimbursement and product orders, along with patient education materials that will assist urologists' and their assistants' interaction with patients. Minimal effort will be directed towards the non-adopters, or laggards.

[7] *Based on QLT primary market research from past several years.*

4.3.2 Healthcare Payors

As mentioned in Section 2.6.2, ~70% of males with BPH are covered under Medicare, the federal payor, governed by the Centers for Medicare and Medicaid Services, or CMS. Other payors of consideration for BPH include managed care that includes Health Maintenance Organizations (HMOs), Preferred Provider Organizations (PPOs) and Managed Care Organizations (MCOs). Adoption among healthcare payors will require that QLT work with the major payors' technical assessment groups following data from Phase II and Phase III to determine or devise clinical endpoints to assess the pharmacoeconomic value associated with Lemuteporfin therapy for BPH. Communication with these groups needs to be focused on clear benefit/risk ratio with economic savings in the treatment of benign prostatic hyperplasia. In addition, identifying key advocates from the urology community who can influence advisory panels reviewing Lemuteporfin therapy will facilitate its integration into treatment guidelines and therefore ease reimbursement for physicians and patients.

4.3.3 Patients

Segmenting the BPH market appropriately and applying specific tactics through a communication and sales force planning effort will be critical to ensuring the greatest penetration into the marketplace. The BPH market consists of those men who have mild, moderate or severe symptoms. Further segmentation for this population illustrates that there are men who have not been diagnosed for BPH and men who have been diagnosed and in turn, fall into the following categories: 1) have not been treated for their BPH, 2) are on medical therapy treatment, 3) have received an intervention for their BPH symptoms with a minimally invasive or invasive procedure or 4) have failed their medical or procedural treatment for BPH.

As illustrated in the Situational Analysis Section, symptomatic BPH patients typically require or receive treatment in the U.S. due to adequate access to healthcare. This fact combined with the understanding that BPH patient flow moves first from the general practitioner's office to the urologist's office in most cases (Chestnut Partnership, 2002) and the treatment armamentarium available to the general practitioner (medical therapy) vs. the urologist (medical therapy and minimally invasive or invasive procedures) suggests that the initial market for Lemuteporfin therapy will be a symptomatic BPH patient who, in the majority of cases, has tried medical therapy first. The rationale for focusing on this market development strategy initially is the reality that a new MIT therapy is only applicable to the urology physician audience, and therefore development efforts should address the BPH market typically seen by urologists. Opportunities for Lemuteporfin therapy to expand beyond this segment of the BPH market into other segments will be driven from a market development strategy to position Lemuteporfin as a first-line therapy for BPH through efforts to target referral networks such as focusing on general practioners to move BPH patients to urologists sooner, and direct-to-patient advertising targeting the diagnosed BPH patient wanting a one-time treatment.

4.3.4 Referral Networks

For referral networks, the main physician focus will be general practitioners who ultimately refer benign prostatic hyperplasia patients to urologists. Adoption of Lemuteporfin therapy will require market segmentation with the general practitioner group to identify who are the high-volume treaters/gate-keepers for benign prostatic hyperplasia patients. Educational meetings sponsored by QLT between community-based urologists and general practitioners will help to develop and maintain referral channels between these groups of physicians.

Using the referral networks, the strategy is to develop Lemuteporfin into a first-line therapy, moving moderate to severe patients away from medical therapy and directly to a one-

time intervention, or MIT. Education and awareness of the patient type appropriate to be treated with Lemuteporfin therapy will be key with this physician audience. The important challenge will to understand what value can be brought to the referral segment in order to convince these physicians from prescribing medical therapy to their moderate to severe BPH patients and referring these patients directly to urologists. A plan to overcome this challenge is presented in the tactical plan. In addition to this strategy, QLT can undertake a strategy to work with thought leaders to influence AUA treatment guidelines and payers to emphasize the benefits of Lemuteporfin therapy as a first-line treatment approach, as the referral physicians with non-extensive experience in treating BPH are more likely to refer to what the recommendations are of these two groups.

4.4 Product Strategy

Lemuteporfin for BPH will consist of both drug and device disposables that will used in the therapy, as well as the capital laser unit that will be required to generate light to activate the drug. The main focus for Lemuteporfin therapy will be the marketing of the drug and device disposable.

In order to ensure QLT's product is competitive in price to alternative MITs and to maximize revenues manufacturing costs and the pricing established for each of the components will need to be controlled and determined by QLT. Offering urologists a bundled package as one brand will establish that the disposable components represent one therapy, Lemuteporfin injectable for BPH. In addition, this "bundling" product strategy will assist with the pricing, distribution, and reimbursement strategies described in the following sections.

4.5 Pricing Strategy

Pricing Lemuteporfin for BPH should follow a sales-oriented pricing strategy instead of a profit-oriented pricing strategy as recouping the cost of significant research and development activities in the short-term under a profit-oriented pricing strategy could be challenging. Following a sales-oriented pricing strategy, it is important to build a broad base of users for the therapy in order to further spread the development and marketing costs.

As Lemuteporfin for BPH will have competitive advantages over alternative MITs, a premium pricing strategy can be employed. However, QLT needs to remain cognizant of the average selling price for disposables of minimally invasive therapies so that the premium price does not pose a barrier for urologists and payors. As mentioned in Section 2.4, the average selling price for disposables for minimally invasive therapies is estimated to be $1,000. Ideally, a price determined by QLT to sell to urologists will be a single price for the bundled package of both the disposable device and drug enabling urologists to use an easier method of billing and administration. Following Phase II clinical results, market research with physicians and payors using the price assumptions will need to be conducted to determine any pricing sensitivities to performance outcomes for Lemuteporfin therapy.

With respect to the capital laser equipment, the strategy for this product will be to ensure that the costs associated with the equipment do not pose a barrier to adoption for urologists. Therefore, the price to be considered for establishing this unit in a urologist's office may be the cost of manufacturing without significant mark-up.

4.6 Promotional Strategy

QLT will use a personal selling strategy through sales force efforts to deliver the product positioning and messages related to the Lemuteporfin therapy in BPH to urologists. The

positioning will need to be clear and the messages targeted in order to clearly differentiate Lemuteporfin from alternative minimally invasive therapies.

4.6.1 Positioning

Within the armamentarium of BPH treatments, urologists interviewed early in development in a qualitative market research study envisioned Lemuteporfin therapy positioned with other minimally invasive therapies rather than against TURP or medical therapy. Most respondents assumed that Lemuteporfin therapy would achieve a better efficacy over medical therapy due to its procedural route of administration but would not achieve the same efficacy as TURP due to its minimally invasive approach, and hence should be positioned within the minimally invasive therapies for BPH.

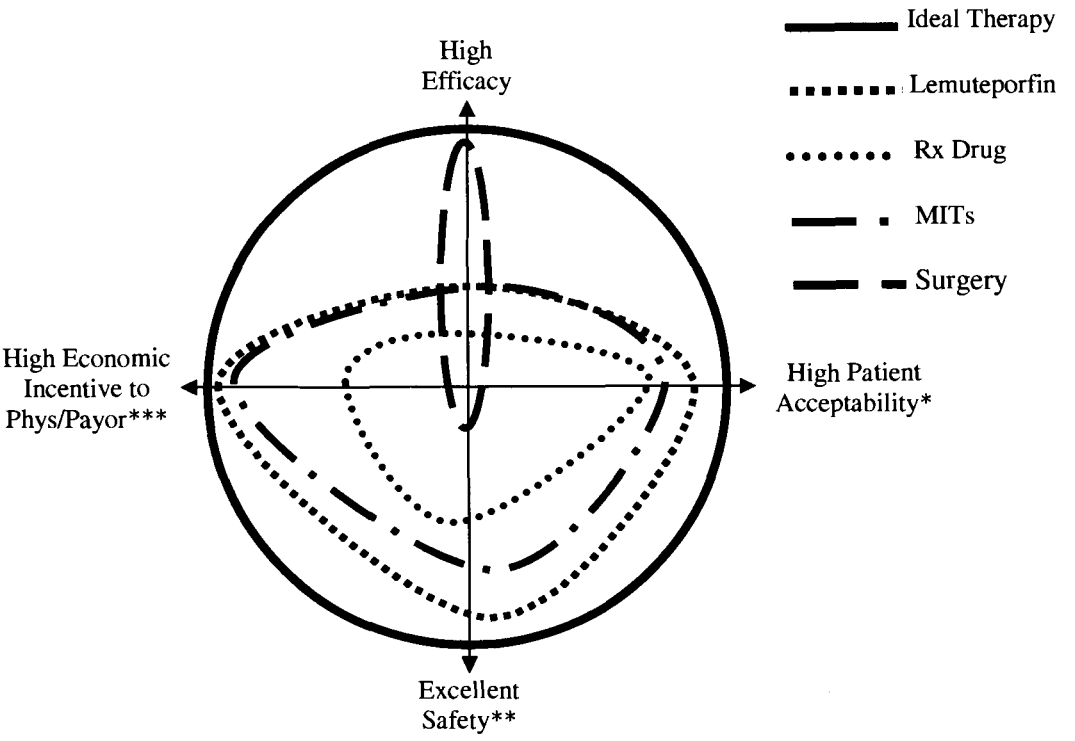
Further market research from urologists interviewed and data from the Phase I/II clinical trial with Lemuteporfin therapy in BPH, uncovered that product attributes such as the time to perform the procedure or the efficiency with the procedure, faster onset of action, less post-procedural irritation, and reduced catheterization events were all product attributes worthy of demonstrating superiority over alternative MITs on the market. These attributes, combined with the BPH patient population that will benefit from a MIT therapy and are the BPH population applicable to the patients of concern to the urologist and the payor, can form a preliminary positioning statement as written below:

Photodynamic therapy with Lemuteporfin is an office-based, minimally invasive therapy that is therapeutically effective in relieving symptomatic BPH using a non-thermal, simple and safe approach that is attractive to patients.

Figure 6 depicts the proposed position for QLT's product combining the overall position for Lemuteporfin therapy among alternative treatments for BPH and the product attributes applicable for a BPH therapy. In this figure, Lemuteporfin therapy is equivalent in efficacy to

alternative MITs but product attributes such as a shorter procedural time with good outcomes related to faster onset of action, less post-procedural irritation and reduced catheterization events provide Lemuteporfin therapy with competitive advantages over the position of alternative MITs.

Figure 6 Positioning of Lemuteporfin Therapy



* Patient Acceptability as defined by no catheterization, faster onset of action and one time treatment.
** Excellent Safety as defined by no irritation, no bleeding and no side-effects.
*** Economic Incentive as defined by reduced hospitalization costs (i.e. office-based procedure) and effective treatment with longer term performance, and a good performance/investment balanced procedure.

Source: Quinn in Collett et al, GEMS™: A Treatment for Obesity, 2004, by permission.

4.6.2 Message Strategy

Once the product positioning for Lemuteporfin therapy is established, this will set the direction for the message strategy and determine which messages will be subsequently

implemented and carried forth in a communication plan. As indicated as one of the Critical Success Factors, the promotional message focusing on usability will be key for a product that demonstrates similar efficacy to alternative MITs on the market. Therefore, the primary message will focus on usability, safety, and cost-effectiveness, factors that contribute to added value over efficacy to the urologist, patient, and payor and are clear competitive advantages over thermal minimally invasive therapies. Supportive messages will assure the urologist, patient, and payor that Lemuteporfin therapy achieves similar efficacy to office-based MITs currently on the market. Revisiting and refining of the message strategy will take place following more clinical data and market research, however, in the interim key messages that will be valuable in development and commercialization activities are listed in Table 2.

Table 2 Lemuteporfin Therapy Key Messages

Usability	
1.1	Lemuteporfin therapy is a safe, targeted procedure that delivers a therapeutic dose for relief of BPH symptoms only when the combination of drug and light are present in the prostate.
1.2	Lemuteporfin therapy rapidly alleviates symptoms related with BPH allowing patients to return to their normal activities within days.
1.3	Lemuteporfin therapy provides therapeutic relief of BPH symptoms without swelling and irritation of the prostate.
1.4	Lemuteporfin therapy improves quality of life for patients, without the need for post-procedural catheterization.

Safety	
1.5	Lemuteporfin therapy is a safe, targeted procedure that delivers a therapeutic dose for relief of BPH symptoms only when the combination of drug and light are present in the prostate.
1.6	Lemuteporfin therapy is a non-thermal MIT procedure negating the need for monitoring intra-prostatic and surrounding tissue temperatures.

Cost-effectiveness	
1.7	Lemuteporfin therapy is performed in a urologist's office in as little as 30 minutes for the entire procedure.
1.8	Lemuteporfin therapy is a one-time, office-based procedure allowing patients to come off drugs for their BPH and negating the need for invasive, more costly treatments for BPH

Efficacy	
2.1	Lemuteporfin therapy delivers significant relief of BPH symptoms compared to medical therapy.
2.2	Lemuteporfin therapy provides therapeutic relief of BPH symptoms similar to alternative minimally invasive modalities using a *non-thermal* approach.

4.6.3 Publication Strategy

Developing a publication strategy assists in creating product and brand awareness. It is envisaged that the strategy will include publications in prominent journals related to benign prostatic hyperplasia and urology that are reviewed by the target physician audience. Clinical and

Marketing teams need to collaborate through Project teams in defining objectives, a plan, and a timeline for targeting peer-reviewed journals. Preliminary objectives related to the publication strategy are to increase awareness with urologists by using consistent messages as outlined in Table 2 to differentiate Lemuteporfin therapy from alternative minimally invasive therapies. Development of a publication plan during Phase II will need to take place in order to target major publications once Phase II data are available. The major publications Clinical and Marketing will need to consider for marketing Lemuteporfin therapy in the U.S. include the Journal of Urology, Contemporary Urology, Urology Times, and the Journal of Endourology. The Journal of Urology is the most significant as it is considered the official journal of the American Urological Association society.

4.6.4 Meetings Strategy

The objective for Lemuteporfin therapy is to have a significant scientific and promotional presence at target urology meetings in the U.S. to create awareness and interest from urologists. Each meeting will require a specific communication plan to deliver Lemuteporfin key messages in the form of poster, plenary, and course sessions as well as roundtable meetings taking place at these major forums. The major meetings in urology where new products in development are presented include the annual American Urological Association meeting and the Urology World Congress. Closer to launch, following interim Phase III data or during pre-registration of Lemuteporfin with the Food and Drug Administration (FDA), communication material developed for exhibit halls, advocacy meetings, and social activities related to major conventions will be key to creating promotional momentum prior to launch.

4.7 Distribution Strategy

The distribution strategy for Lemuteporfin therapy in BPH will follow a "push" strategy to get urologists to ask for the product directly from QLT, if QLT chooses to pursue a direct channel of distribution for Lemuteporfin therapy, or through intermediaries who may be involved in supplying urologists with the product. Efforts will need to be made to coordinate the distribution of both drug and device disposables to simultaneously reach the urologists office if the two components are not physically packaged together. Ideally, one "bundled" product package will mitigate any loss of either drug or device disposable in the supply chain.

Lemuteporfin should be distributed directly by QLT as this will maximize the margins to both QLT and the physician. To put this into perspective, in this hypothetical situation, a urologist may be reimbursed $4,000 for a MIT therapy where the disposables and miscellaneous expenses (assistant's time, standard office medications used, administrative time, etc.) for performing this therapy costs may cost approximately $1,500, so the urologist makes an estimated return of $2,500 for his time in performing the procedure. In order for Lemuteporfin to remain competitive, the total cost for performing the procedure needs to be approximately the same amount as alternative minimally invasive therapies, therefore the more channels in the supply chain necessary to distribute the product either means an increase in the price to account for this or a decrease in the margin back to QLT on the product.

However, if the product requires an intermediary to distribute the product to increase coordination efforts, a specialty or exclusive distributor should be contracted to manage these activities. This will minimize the risk of confusion as distribution of the product will be centralized and the distributor will place a greater emphasis on the timely shipping of the product as QLT can offer a greater percentage on the mark-up of the product to an exclusive distributor as compared to many distributors taking a portion of that mark-up.

4.8 Reimbursement Strategy

The goal of reimbursement for Lemuteporfin will be to provide an incentive for the urologist and the patient to use the therapy for BPH. Metrics for reimbursement will be an inter-play of various components including competitive factors affecting the price for QLT's therapy, the clinical performance outcomes from Phase II and III, the usability of the therapy, and the long-term data generated to support durability of the therapy as a one-time procedure. Overall, adequate reimbursement must be established early on in the launch of Lemuteporfin therapy to ensure that no barriers to adoption take place among physicians and patients. QLT will need to coordinate the efforts of marketing and clinical internally to provide the necessary data for demonstrating a pharmacoeconomic benefit to healthcare payors.

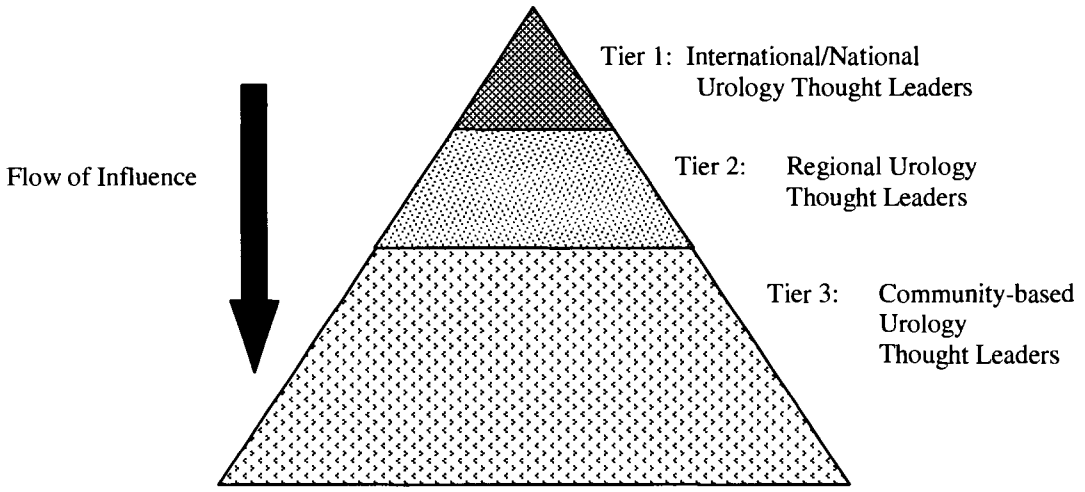
4.9 Thought Leader Development Strategy

Thought leaders in clinical development represent a valuable opportunity for creating awareness and trial for a new product. For QLT Inc., thought leaders will play a critical role in communicating the benefits of Lemuteporfin therapy to a wider community-based audience through speaking sessions, reviewing and authoring publications and training other urologists, as seen in Figure 7. Nationally and internationally known thought leaders, or Tier 1 physicians, such as Dr. John McConnell from Cornell University and Dr. Claus Roehrborn from Southwestern Medical Centre, University of Texas Southwestern are leading experts on treatments for benign prostatic hyperplasia.[8] Involvement of these thought leaders in some capacity throughout the development program is important to gaining buy-in from these leaders for the therapy and influencing a broader audience of users who refer to these experts for guidance on new therapies in benign prostatic hyperplasia. Identifying and mapping out key

[8] *Notable urologists seen presenting at meetings the author attended during urology conferences in the past couple of years.*

physicians at each level - Tier 1, 2, and 3 - will help to focus marketing efforts to attracting these physicians prior to launch.

Figure 7 Peer Influence for Thought Leaders in Urology



Based on Report by QLT Inc., Tariquidar Marketing Plan, 2003.

5 TACTICAL PLAN FOR LEMUTEPORFIN

The tactical plan addresses the essential activities required both pre-launch and post-launch to maximize the exposure and awareness of Lemuteporfin in BPH with the target market consisting of urologists, patients, and payors. The tactical plan combines the elements of the marketing strategy to achieve the desired positioning of Lemuteporfin in BPH.

5.1 Pre-launch Tactics

5.1.1 Thought Leader Mapping and Customer Segmentation

To achieve wide acceptance of Lemuteporfin in BPH among urologists in an efficient manner, a target list of thought leaders needs to be determined who have national and regional influence over prescribing behaviours with community-based urologists. Those thought leaders who are identified can be used in publication planning, speakers training and alternative advocacy forums.

Prior to Phase III clinical development, a market research vendor should be sourced and commissioned to conduct a thought leader mapping study across the U.S. The study consists of a simple questionnaire asking a projectable sample of urologists whose opinion they consider when needing advice on a new therapy for BPH. These questions are directed towards finding thought leader names on both a national and regional level. The results of the study are used to develop a list of tier 1 and 2 urologists based on the frequency of names cited throughout the study.

In parallel to conducting the thought leader mapping, a customer segmentation study is required to determine the top prescribing urologists in group and single practice settings. Claims

data from alternative minimally invasive therapies tracked via zip codes to urologists practices will identify the top prescribers of MITs. These data combined with a study to determine the attitudes and behaviours of these urologists to new modalities for benign prostatic hyperplasia will provide sales personnel with a targeted customer list as well as information to create customized sales tactics to influence prescribing behaviours. In addition, the targeted customer list will increase efficiency in the placement of the capital laser equipment for Lemuteporfin therapy in key urological practices where a significant number of benign prostatic hyperplasia is treated.

5.1.2 Key Marketing Personnel

Once a target list of national and regional thought leaders is developed, internal efforts should be directed towards coordinating the key messages between the external (i.e. thought leaders) and the internal facilitators (i.e. marketing and clinical managers, and sales personnel) for launching Lemuteporfin in BPH and creating awareness. A key member of the internal team who will act as the cohesion between these groups is the Medical Marketing manager.

The Medical Marketing manager will be responsible for creating the promotional materials such as slide kits for major meeting presentations, sales aids used throughout personal promotion and patient educational material for direct to consumer advertising with the collaboration from clinical, marketing, and thought leaders. It is important that the Medical Marketing manager becomes part of the Lemuteporfin in BPH clinical development program before Phase III commences. Many of the key activities such as publication submissions and meeting preparations will take place following data from Phase II.

Anticipating any barriers to use with Lemuteporfin and urologists and addressing these prior to launch is essential to a smooth launch for the product. Reimbursement of the product and

therapy is necessary in order for urologists to not only trial the therapy but continue using it. The hiring of a Reimbursement Manager after Phase II clinical data are received will need to take place in order for efforts to be directed toward developing a reimbursement plan and coordinating relations between QLT and the Centers for Medicare and Medicaid Services (CMS) in the U.S. with the objective of establishing a product/therapy reimbursement code and an appropriate reimbursement amount for urologists/QLT/CMS prior to launch.

The Reimbursement Manager will need to work with clinical, management, and external consultants to incorporate any pharmacoeconomic variables into the Phase III clinical trial design that will demonstrate the cost-effectiveness of Lemuteporfin therapy. Prior to pharmacoeconomic data becoming available, the Reimbursement Manager will need to coordinate QLT meetings with CMS in the early stages of Phase III. This will enable QLT to begin establishing a relationship with the agency and to make the agency aware of Lemuteporfin therapy. By doing so, this prepares CMS to begin addressing the economic impact of Lemuteporfin therapy to the healthcare budget when the product is launched.

5.1.3 Pricing and Reimbursement for Lemuteporfin

Lemuteporfin will be considered a minimally invasive therapy for BPH and therefore will be an alternative to already established MITs on the market. Pricing Lemuteporfin will be an important undertaking for QLT and will need to be thoroughly researched with urologists and payors in order to effectively price the therapy so that it is widely accepted in the marketplace.

During Phase III clinical development following an interim analysis of the data (i.e. at six months), a pricing study will need to be conducted by a market research vendor with urologists. Typically these studies are a conjoint analysis, determining the product attributes that are most desirable and the price elasticity around these attributes when they are substituted. This study

will need to compare Lemuteporfin with alternative MITs and determine the premium that can be set for added value benefits associated with Lemuteporfin such as the non-thermal, simple, and safe approach to treating the prostate.

Information from the pricing research, forecasts for the number of procedures, reimbursement of thermal minimally invasive therapies, and the anticipated benefits of Lemuteporfin over alternative minimally invasive therapies will need to be crafted into a pricing model and cost/benefit analysis that can be used in discussions with third party payors such as the (CMS) when negotiating the level of reimbursement. Discussing these pricing data from the pricing research during phase III development prior to launch will help create a transparent discussion with payors and ensure that reimbursement is established at launch as not to affect product uptake with urologists.

In addition to negotiating the level of reimbursement for Lemuteporfin, a justification will need to be made for Lemuteporfin, although a combination drug/device disposable, to be treated as a "one product" or "bundled product" code when urologists bill for the procedure. Benchmarking and gathering the codes for alternative minimally invasive procedures will help QLT in receiving this designation and ease reimbursement for the end-user.

5.1.4 Branding

Branding for Lemuteporfin will be an important tactic for QLT in exemplifying the benefits associated with the product and creating awareness throughout clinical development. Branding will include activities such as determining a product name, a logo and a package that will be used in publications, training/educational materials, sales aids, and patient brochures. Finding a brand image for Lemuteporfin will help lay down the design foundation for the promotional campaign.

Branding will begin with QLT enlisting the services of an advertising agency and working with the company to develop a few prototype brands. Once a list of brands is determined, it will be important to review these brands for conflicts with registered trademarks or other established brands to determine if there is any possibility for confusion or misinterpretation. Next, concept tests in focus group settings will need to be conducted with urologists and the branding prototypes to determine what attitudes and behaviours are elicited from each prototype.

After a brand is chosen based on the market research conducted, and with the agreement within the product team at QLT, this brand will need to be incorporated into all publications for Lemuteporfin for BPH. Ideally, finding a brand and the associated logo and images with that brand will need to be undertaken once phase II data are available as this will increase the exposure of the brand into major publications prior to launch.

5.2 Post-launch Tactics

5.2.1 Practice Management Support

Ease of use for Lemuteporfin with urologists is critical to its adoption. A practice management software tool would be useful to assist urologists in efficiently treating patients with benign prostatic hyperplasia with Lemuteporfin. The software should address how to effectively manage the key practice drivers for urologists: product orders and delivery; scheduling of patients to be treated with Lemuteporfin; and handling and tracking of reimbursement claims. The software will need to be compatible with a urologist's office dynamics and easily managed by staff employed at a urology practice.

Methods that can be used to develop a software package that will be adaptable to urologists include preceptorships where marketing and clinical staff can witness first-hand the patient flow and practice dynamic within a practice. Following this initiative, a software

prototype can be developed by practice management specialists with experience in developing pharmaceutical practice tools and tested with a group of urologists from several different regional areas used to give the software a "dry-run" and provide any suggestions for changes. Dissemination and training on the practice management software will be conducted by sales personnel actively promoting Lemuteporfin.

5.2.2 Post-Marketing Clinical Studies

The objective of post-marketing clinical studies is to provide urologists, possibly those who were not involved throughout the development plan, with an opportunity to conduct smaller scale clinical studies that attempt to improve on the efficacy, efficiency, and/or cost-effectiveness of Lemuteporfin therapy. Prior to any investigator-initiated or clinician driven study, QLT will need to review the protocol of the study to ensure that the objectives of the study will provide QLT with strategic value. Following agreement on the design of the study and plans to go forward with it, QLT will need to provide access to free drug for these investigators treating patients.

A valuable example of a post-marketing study currently being conducted by the National Institute of Health looks at the long-term effectiveness comparing three types of therapy: combination medical therapy with an alpha blocker and 5-alpha reductase inhibitor, transurethral microwave thermotherapy, and transurethral needle ablation therapy (National Institutes of Diabetes & Digestive & Kidney Diseases, or NIDDK, 2004). The study will follow patients for five years and compare efficacy between the three modes of treatment and retreatment rates. This clinical study has the potential to demonstrate that a one-time treatment with an MIT is cost-effective over daily dosing with medical therapy.

It will be advantageous for QLT to follow Phase II clinical trial patients for five years and report on efficacy and retreatment rates to allow urologists and payors to compare Lemuteporfin data with the data generated from the NIH trial and determine cost-effectiveness to their practice or budgets, respectively. Patient registry data collected from urologists selected to participate post-launch outside of the clinical development of Lemuteporfin can also provide valuable pharmacoeconomic data that can be used to compare Lemuteporfin to the treatment modalities chosen in the NIH trial.

5.2.3 Training Program for Lemuteporfin Therapy

Following the launch of Lemuteporfin therapy, a training program throughout the U.S. will need to be deployed to develop trial of the product by the early majority therefore capturing the momentum by this group to successfully launch the product. Detailed plans for the training program will have already taken place in Phase III clinical development by personnel from marketing, clinical, and device engineering. Regional implementation of the training program will take place with the participation of trained medical liaisons, sales personnel, and previous clinical investigators for Lemuteporfin. In practice, Continuing Medical Education (CME) sessions are best utilized to address any challenges with a drug/device procedure for benign prostatic hyperplasia and master the procedure. Regional centres of urological expertise can be identified and used to invite community-based urologists to witness first-hand a patient being treated with a MIT procedure with Lemuteporfin therapy.

During the first several months post-launch, sales personnel will be fully deployed to attend the first few treatments with Lemuteporfin therapy at urology customers' practice. Investment into this personalized training and support will be critical to increasing the comfort level of urologists thereby facilitating continued use and potential for customer loyalty with using Lemuteporfin therapy in addition to "ironing" out any difficulties with performing the procedure

in the beginning, mitigating any potential problems that may occur if urologists attempted to treat the patient without any support from the sales team at QLT.

5.2.4 Establishing Referral Networks

Establishing referral networks between general practitioners and urologists begins with QLT sales personnel demonstrating to urologists the economic gain in using Lemuteporfin therapy and providing urologists with the data to present to their general practitioner community that illustrate that the costs of managing benign prostatic hyperplasia (frequent visits requires practitioner's time) outweighs the benefits (office visit reimbursement is minimal). Investing in these tools will help QLT in growing the overall patient population for Lemuteporfin therapy.

Financial models created internally at QLT can place into perspective the number of patients a urologist will need to treat to move beyond the threshold costs associated with the drug/device disposable and capital device. From here, a urologist will be motivated to educate general practitioners in their community in identifying the appropriate symptomatic BPH patient to refer as continued treatment of this patient with medical therapy would not significantly improve his symptoms and therefore a procedural based treatment, performed only by a urologist, may be necessary.

5.3 Implementation

Although the details of the expenses, financial projections and timing of the execution plan will not be shared in this marketing plan that is intended for publication, the version intended for internal use at QLT will include these details in order to make the marketing plan complete. Today, based on the fit of Lemuteporfin therapy with QLT's business strategy and the markets it intends to pursue, the financing of the marketing plan will be undertaken by QLT and will add to QLT becoming a fully-integrated biopharmaceutical company with both development and

marketing capabilities. Lemuteporfin therapy is an integral development opportunity for QLT and as such, QLT is committed to move forward with this program as it achieves its developmental milestones.

5.4 Definition of Success

Upon launch of Lemuteporfin therapy, defining success will be in terms of market penetration, market share and sales revenues. Market penetration will include factors such as number of urologists adopting the therapy and number of patients treated. Market share will consist of percent of sales and procedures of overall minimally invasive therapy market. QLT internal targets for sales revenues of Lemuteporfin will be set prior to launch to prioritize the resources to QLT's pipeline of products and to provide motivation to the sales team assigned to Lemuteporfin. In broad terms, a product that achieves a 10-25% market share in a growing market that is not yet saturated is considered achievable and reasonable for Lemuteporfin given its advantages over current MITs. Based on the current commercialized products at QLT, Eligard® and Visudyne®, sales revenue targets of Lemuteporfin can be expected to achieve peak sales levels between $100 M and $500 M to warrant QLT's financial commitment to developing the program for BPH.

6 CONCLUSIONS

The market for Lemuteporfin as a minimally invasive therapy in benign prostatic hyperplasia is present and growing. The features of Lemuteporfin, compared to alternative MITs, coupled with the growing trend to use office-based procedures compared to expensive hospital procedures or long-term medical therapy use, make it attractive to QLT to commercialize its third-generation PDT drug as a product intended for the BPH market.

Identifying a strategic position for a product is critical to its success. As we can see with Lemuteporfin, there are opportunities for the product to be positioned in different ways to accomplish two different strategic objectives: competing effectively with current MITs and growing the BPH market. In this plan, product attributes of Lemuteporfin, such as usability, are used to assist the product in penetrating the MIT marketplace and focusing on this product as a first-line therapy to grow and to develop the market for minimally invasive therapies.

Building relationships is a key message resonating throughout the marketing plan for Lemuteporfin. It is outlined in the strategies and tactics to attract users by focusing on a top-down approach information dissemination, or tiers of influence among urologists, where thought leaders and clinical investigators for Lemuteporfin communicate the product messages of Lemuteporfin to community-based urologists. In terms of formalizing reimbursement for Lemuteporfin, forming a relationship between QLT and the Centers for Medicare and Medicaid Services in Phase III clinical development is important to ensuring success with the product's uptake with its users. These relationships with customers are important to create awareness for Lemuteporfin and in turn, to gain buy-in for the product from both product performance and benefit/cost perspectives.

7 APPENDIX: AUA SYMPTOM INDEX QUESTIONNAIRE

	Not at All	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost Always	
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?							
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?							
3. Over the past month, how often have you found you stopped and started again several times when you urinated?							
4. Over the past month, how often have you found it difficult to postpone urination?							
5. Over the past month, how often have you had a weak urinary stream?							
6. Over the past month, how often have you had to push or strain to begin urination?							
	None	1 time	2 times	3 times	4 times	5 or more times	
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?							
						Total Symptom Score	

Source: Roehrborn et al., American Urological Association, BPH Patient Guide, 2003, by permission.

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