

# **PROTON/CARBON CANCER TREATMENT BUSINESS CASE**

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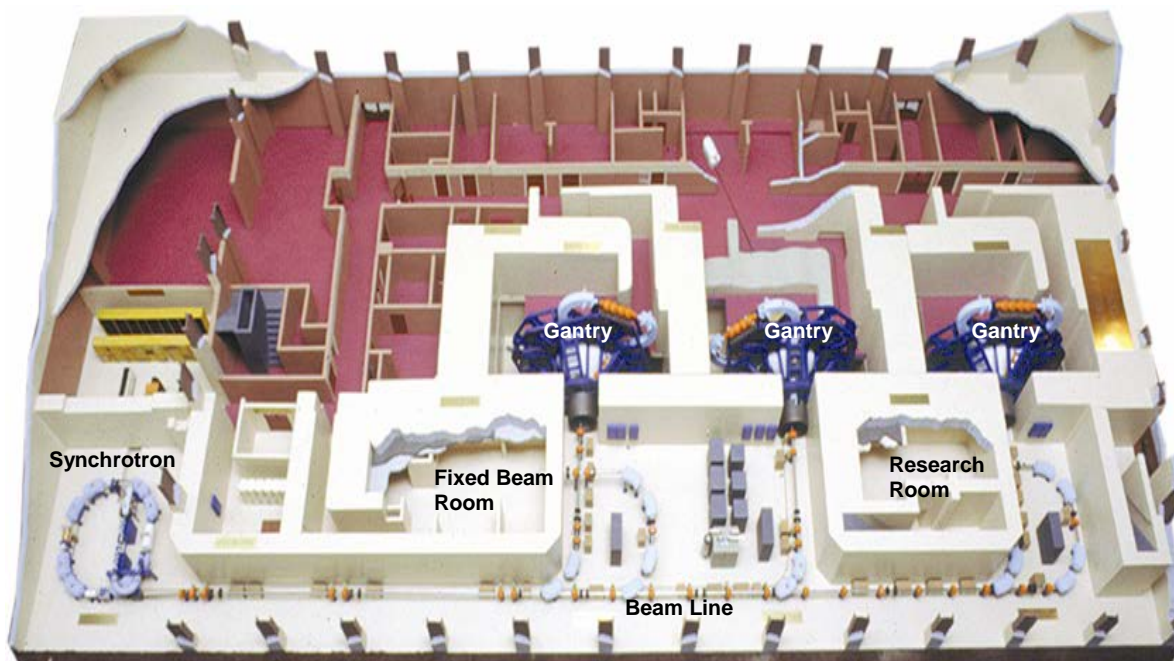
## BUSINESS CASE

### Background

Historically, proton therapy equipment solutions have been designed to use a single accelerator, cyclotron or synchrotron, to accelerate charged particles to near the speed of light. These particles are then directed to multiple treatment rooms via a beam line outfitted with focusing, switching and steering magnets, ostensibly to spread the capital cost of the accelerator over multiple treatment rooms. Each treatment room is equipped with a stationary or fixed beam port or a large superstructure called a gantry. The physical characteristics of particle therapy dictate that the gantry diameter is in excess of 30 feet. Further, the gantry must be capable of supporting multiple steering magnets, each weighing several tons. While the use of a gantry permits the delivery of the beam from any angle enhancing system flexibility, it adds considerably to the equipment cost and facility size. Throughout the process the particle beam is maintained under vacuum conditions.

All currently commercially available products are based on this multi-room design philosophy. The equipment component of a multi-room proton therapy treatment center carries a price of \$50-100+M. The large size of this equipment typically dictates the construction of a new building to house the treatment center ranging in cost from \$20-40M. A typical multi-room treatment center, as illustrated in Figure 1 requires a footprint of 300 feet by 200 feet with the treatment room section consuming 3 floors of vertical space. Architectural design, construction, equipment installation and commissioning typically require 3 years to complete.

**Figure 1: Model of Loma Linda University Proton Therapy Center.**



Several companies have begun efforts to develop a single room design proton therapy product in an attempt to lower the barrier of entry for proton therapy. One such development stage company, Still River Systems, has secured orders for 8 systems in 2006 and 2007.

Our mission is to serve as a catalyst for change in the health care of cancer patients through a concerted effort to build an international network of proton therapy centers in strategic locations. We recognize the largely unmet demand for the ability to provide particle therapy services from many healthcare institutions both domestically and internationally. While other companies have been established in an effort to satisfy the multifaceted demands for proton therapy, our model is distinctly different from other commercial efforts.

The National Cancer Institute (NCI), a component of the National Institutes of Health, was established by virtue of the National Cancer Act of 1937 to serve as the Federal Government's primary agency for cancer research and training. The NCI's scope was expanded by the National Cancer Act of 1971 in which the National Cancer Program was created. This NCI managed program conducts and supports research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer, rehabilitation from cancer, and the continuing care of cancer patients and the families of cancer patients – a comprehensive approach to cancer. To foster advances in cancer care and research the NCI has created a competitive evaluation process to create a “best of the best” two tier designation – Comprehensive Cancer Centers (41) and Cancer Centers (22).

## **The Market**

The global market for radiation therapy is large and growing. Research conducted by The International Agency for Research in Cancer (IARC) indicates that 10.9 million new cancer patients were diagnosed in 2002. Further, the IARC estimates that this will grow to over 16 million in 2020. Leading particle therapy researcher Gerhard Kraft, PhD, Gesellschaft für Schwerionenforschung (GSI) in Darmstadt, Germany has published data indicating that 18% of cancer patients ultimately die from local control failure. Dr. Kraft's position is that existing cancer therapies, including conventional photon radiation therapy, fail to cure these patients, making them ideal candidates for particle therapy. Treating this world-wide sub-group of 1.9 million annual cancer patients would require in excess of 3,900 particle therapy treatment rooms. There are approximately 50 treatment rooms in operation today, across the globe.

Each treatment room represents a capital investment of approximately \$20M for a proton therapy only technology solution. The capital investment required for a multi-room proton + heavy particle technology solution can exceed \$150M. This represents a global market in excess of \$75B for one time particle therapy technology equipment sales.

Table 1 presents conservative financial projections developed by PTI for clinical proton therapy performed by a 4 Room Facility. These projections presume that each treatment room is operating 5 days per week, 12 working hours per day. Facility capacity can be expanded by offering extended and weekend hours. These projections were extrapolated to present projections for a 1 Room Facility and to demonstrate the Total U.S. Market potential for clinical proton therapy based on American Cancer Society cancer projections for 2008. This data presents a compelling business case in support of proton therapy and provides a financial explanation for the explosive growth taking place in this industry.

**Table 1: Annual Financial Projections for Proton Therapy Treatments.**

|                                        | <b>1 Room Facility</b> | <b>4 Room Facility</b> | <b>Total U.S Market</b> |
|----------------------------------------|------------------------|------------------------|-------------------------|
| <b>Projected Proton Patients</b>       | 400                    | 1,600                  | 258,692                 |
| <b>Approximate Revenue per Patient</b> | \$55,000               | \$55,000               | \$55,000                |
| <b>Total Revenue</b>                   | \$22,381,500           | \$89,526,000           | \$14,474,787,495        |
| <b>EBITDA</b>                          | \$14,557,525           | \$58,230,100           | \$9,414,788,143         |
| <b>Operational Cash Generation</b>     | \$10,183,925           | \$40,735,700           | \$6,586,249,815         |

Table 2 provides information regarding the five existing locations where comprehensive proton therapy is currently clinically available in the United States.

**Table 2: Existing U.S. Proton Therapy Centers.**

| Institution                      | Location         | 1 <sup>st</sup> Patient | Vendor     | Partner | '07 Patient Estimate | Capacity Estimate |
|----------------------------------|------------------|-------------------------|------------|---------|----------------------|-------------------|
| Loma Linda University            | Loma Linda, CA   | Oct. 1990               | Hybrid     | None    | 2,000                | 3,000             |
| Massachusetts General Hospital   | Boston, MA       | Nov. 2001               | IBA        | None    | 1,000                | 2,000             |
| Midwest Proton Radiotherapy Ins. | Bloomington, IN  | Feb. 2004               | Hybrid/IBA | None    | 500                  | 2,000             |
| MD Anderson Medical Center       | Houston, TX      | May 2006                | Hitachi    | ProBeam | 900                  | 3,500             |
| University of Florida            | Jacksonville, FL | Aug. 2006               | IBA        | None    | 800                  | 2,500             |
| <b>Totals</b>                    |                  |                         |            |         | <b>5,200</b>         | <b>13,000</b>     |

If the existing proton therapy infrastructure in the U.S. were operating at capacity, it could only provide this potentially life saving treatment to less than 5% of the patients suffering with cancers that are in the local control failure category. It is important to note that the existing proton therapy infrastructure is operating far from capacity. This occurrence is due to a number of reasons:

- Grant funding – Loma Linda University and Massachusetts General Hospital are research oriented programs funded primarily by grant dollars.
- Equipment limitations – The Indiana, Texas and Florida centers are still in the process of completing equipment installation, calibration and validation, severely limiting patient capacity.
- Limited working hours – none of the existing facilities treat patients 2 working shifts per day or 6 days per week.

We have identified 15 proton therapy center projects, with a total of 37 treatment rooms, under serious consideration in the U.S. Only 3 projects are under construction; in Philadelphia, Oklahoma City and Hampton, VA. Of these projects, 8 have been announced with the intent to utilize future, single room technology. Combining the capacity of the 5 existing proton therapy centers and the announced 15 potential additional future proton therapy centers will enable the annual treatment, after 2011, of approximately 27,856 of the 260,086 local control failure patients – approximately 11% of the national market. Due to existing and growing patient demand, and a severe infrastructure shortage, proton therapy is a rationed service with expectations that it would remain so for many years to come.

The market for proton/particle therapy equipment is directly related to a number a factors:

- Cancer afflicts a large number of patients – over 10.9M globally and over 1.4M in the U.S.
- Cancer is a growing problem – 16M patients are projected globally in 2020.
- Despite its side effects, conventional radiation therapy is an accepted method for the local control of cancer and is applicable to approximately 50% of all cancer patients.
- Conventional cancer treatment methods fail to provide local control in approximately 18% of all patients.
- Proton/particle therapy's greater effectiveness through increased conformality and relative biological effect and decreased integral dose and incidence of side effects make it ideally suited for the 18% sub-market of cancer patients.
- Clinicians are incentivized to use proton therapy due to its increased effectiveness and high reimbursement level.
- The need and demand for proton therapy far exceeds the available infrastructure.

- Self educated patients recognize the inherent benefits offered by proton therapy and go to great lengths to secure this treatment option.

The confluence of the above points has created a substantial market for proton therapy equipment. Management estimates that the U.S. market for proton therapy equipment exceeds \$10B in one time equipment sales plus approximately \$1B in annually recurring revenue for equipment maintenance. They estimate that the global market for proton therapy equipment exceeds \$75B in one time equipment sales plus approximately \$7B in annually recurring revenue for equipment maintenance.

## Reimbursement

It is realized that regardless of the benefits presented by proton therapy and the resultant demand for this treatment option, without reimbursement, nothing happens. The Centers for Medicare and Medicaid Services (“CMS”) has provided reimbursement for proton therapy since 1997.

CMS is an agency in the U.S. Department of Health & Human Services with a budget of approximately \$650 billion serving approximately 90 million beneficiaries. As CMS is the largest consumer of healthcare services in the world, it is the driving force behind widespread reimbursement for healthcare services in the U.S.

CMS’s dual mission of improving healthcare quality while also lowering cost requires CMS to expend considerable resources in the constant evaluation and re-evaluation of health care technologies and their impact on the overall healthcare system. This requires CMS to probe beyond the initial cost of a healthcare service or drug to also evaluate the long term impact on the healthcare system and overall economy. In this vein, CMS considers the overall economic impact of improved quality of life, long term mortality data and the impact of side effects on long term worker productivity.

According to the National Institutes of Health, in 2007 the overall financial costs associated with cancer totaled \$219.2 billion in the U.S. The financial costs stemming from cancer are detailed in Table 3.

**Table 3: Financial Costs of Cancer.**

| Category                                 | Amount                 |
|------------------------------------------|------------------------|
| Direct Medical Costs                     | \$89 billion           |
| Lost Productivity due to Illness         | \$18.2 billion         |
| Lost Productivity due to Premature Death | \$112 billion          |
| <b>Total</b>                             | <b>\$219.2 billion</b> |

CMS’s evaluation of proton therapy during the 1990’s resulted in the establishment of reimbursement for proton therapy beginning in 1997. As more data has been provided by early adopters of proton therapy, primarily Loma Linda University and Massachusetts General Hospital it is interesting to note that CMS reimbursement for proton therapy has been maintained at a high level for over 10 years. In 2008 CMS is paying \$977.09 per treatment session. Each patient receives 20-40 treatment sessions depending on the type, stage and location of the tumor. In the course of patient treatment, proton centers generate additional revenue through treatment planning, imaging and a variety of other services.

It is important to remember that CMS is an agency of the U.S. government. The process by which CMS sets reimbursement levels is a public procedure and open to comment by the public at large. This creates

an important vehicle through which providers of proton therapy can have a positive influence on proton therapy reimbursement levels.

While CMS is the driving force behind healthcare reimbursement in the U.S., the strong demand for the benefits offered by proton therapy has created an additional reimbursement opportunity – medical tourism. Our market research indicates considerable demand for proton therapy from both domestic and international patients that are wealthy and willing to pay cash for the benefits provided by proton therapy. As an example, our research has indicated that Massachusetts General Hospital limits their international patients to approximately 20% of the patient population treated.

## **Cancer Patient Data**

We recognize that the demand for its initial product offering is driven by the global need to treat cancer patients. We have used data compiled by world renowned and independent organizations, institutes and researchers in an effort to develop an unimpeachable basis for its business plan. Patients with a recent diagnosis of cancer represent a compelling market opportunity – so compelling that a review of independently developed cancer statistics and projections obtained is warranted.

The French based International Agency for Research in Cancer (IARC) is a division of the World Health Organization. The mission of the IARC is to conduct global research on cancer epidemiology, environmental carcinogenesis and research training. The IARC has published research stating that 10.9 million new cancer patients were diagnosed globally in 2002. Further, the IARC has estimated that the global annual incidence of cancer will grow to over 16 million in 2020.

For the U.S., a review of data provided by The American Cancer Society is warranted:

- Over 10.8 million Americans have a history of cancer.
- 1,437,180 newly diagnosed patients were projected for 2008.
- 565,650 deaths due to cancer were projected for 2008.
- Typically 50% of cancer patients are candidates for radiation therapy – based on the above projections this represents 718,590 radiation therapy patients annually.

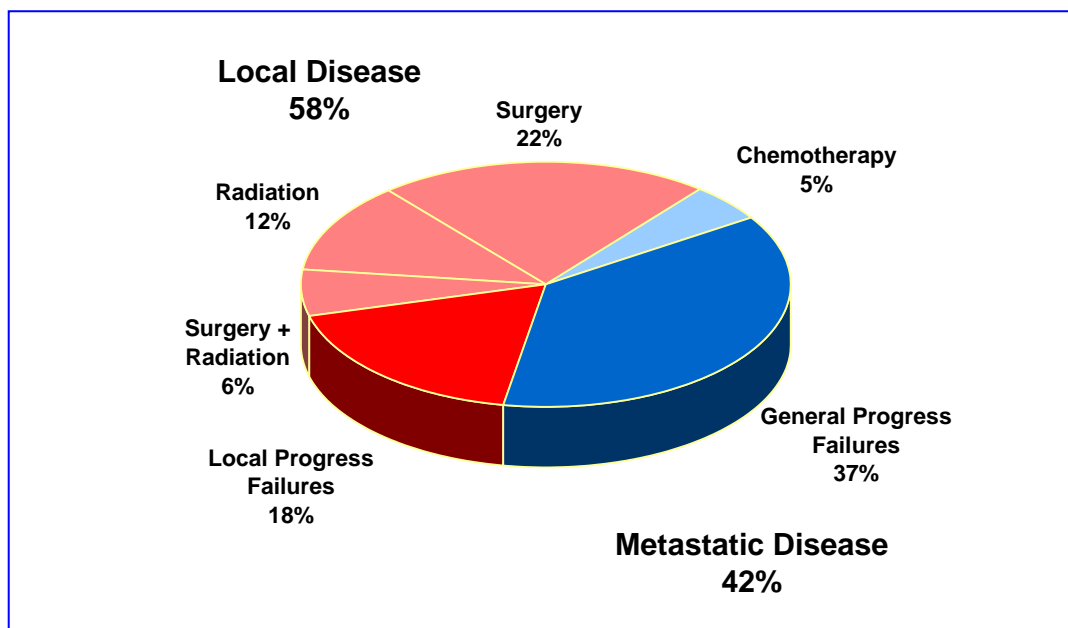
The position of some proponents of proton therapy is that all candidates for radiation therapy would benefit from proton therapy. However, due to severe limitations in the number of facilities providing proton therapy, this potentially life saving technology is usually applied selectively to the patient groups that stand to benefit the most. In this context, proton therapy is likely to be used as a complementary tool for decades to come.

Extensive epidemiological studies have been conducted by researchers in an effort to accurately prioritize cancer indications that would benefit most from particle therapy. While this data will prove important as the particle therapy infrastructure grows to meet patient demand, it is suggested that the patient market for proton therapy is guided by a more basic premise; while currently available cancer treatment methods are effective for many cancer patients, these same methods fail for a significant number of patients. This premise has been presented by multiple researchers. For the sake of this document we have focused our business case on the multiple publications by leading particle therapy researcher Gerhardt Kraft, PhD, Gesellschaft für Schwerionenforschung mbH (GSI) in Darmstadt, Germany.

Dr. Kraft has published data indicating that 18% of cancer patients ultimately die from local control failure; i.e. the failure to kill the tumor while it is in a contained state, allowing it to spread and ultimately resulting in the death of the patient. Dr. Kraft's position is that existing cancer therapies, including conventional photon radiation therapy, fail to cure these patients, making them ideal candidates for particle therapy. As illustrated in Figure 2, Dr. Kraft has observed that roughly 58% of cancer patients

suffer from localized disease (a single tumor at the time of diagnosis) while the remaining 42% of cancer patients at the time of diagnosis suffer from general progress (metastatic disease). A troubling observation made by Dr. Kraft is that 18% of all cancer patients present with local disease, yet currently available treatment methods fail, ultimately leading to their death. Dr. Kraft has repeatedly stated that these patients are the ideal candidates for particle therapy. This is the so called “target market” for particle therapy.

**Figure 2: Distribution of Treatment Methods for Cancer – Kraft.**



Applying Dr. Kraft’s 18% figure to American Cancer Society’s projection that 1,437,180 new cancer patients will be diagnosed in 2008 presents a disturbing result:

- 258,692 of the cancer patients projected to be diagnosed in the U. S. in 2008 will die due to local control failure despite the best treatment methods available today.

The five existing proton therapy centers in the U.S. can provide treatment to less than 5% of this patient segment, creating a huge volume of unmet demand. Since 76% of cancers are in people age 55 and older, the need for particle therapy is expected to continue to grow due to the aging of The Baby Boomer Generation. In all likelihood, decades will pass until the particle therapy infrastructure will be developed to the point at which particle therapy supply will be capable of meeting the demand for this service. This represents an annual U.S. market potential of approximately \$10 billion in revenue for treating patients with proton therapy. The situation is even more dire when examined on a global basis; the existing capacity could treat less than 1% of the patients suffering with cancers that are in the local control failure category – patients with no hope for a successful outcome.

### **Demand for Equipment**

The combination of better treatment outcomes, existing reimbursement, strong patient demand and extreme limits in the existing treatment infrastructure creates a compelling opportunity. A single proton therapy treatment room, operating 12 hours per day, 5 days per week has the capacity to provide treatment for approximately 500 patients per year. Applying this factor to the target market of 18% of all cancer patients gives an indication of the severe shortage of proton therapy equipment.

Treating this world-wide sub-group of 1.9 million annual cancer patients would require in excess of 3,900 particle therapy treatment rooms. Globally, there are approximately 50 treatment rooms in operation today – less than 1% of the number of treatment rooms required today. In the U.S. the existing infrastructure can treat less than 5% of the patients in need. As the incidence in cancer grows, so grows the need for this technology. Each treatment room represents a capital investment of approximately \$20M for a proton therapy only technology solution. The capital investment required for a multi-room proton + heavy particle technology solution can exceed \$150M. This represents a global market in excess of \$75B for one time particle therapy technology equipment sales.

Due to existing and growing patient demand, and a severe infrastructure shortage, proton therapy is a rationed service and is expected to remain so for years to come. This has created an enormous demand for proton therapy technology. We have identified 15 proton therapy center projects, with a total of 37 treatment rooms, under serious consideration in the U.S. illustrated in Table 4.

**Table 4: Announced U.S. Particle Therapy Projects.**

| <b>Institution</b>                                            | <b>Location</b>    | <b>Planned Open</b> | <b>Vendor</b> | <b>Business Partner</b> | <b># of Rooms</b> | <b>Annual Capacity</b> |
|---------------------------------------------------------------|--------------------|---------------------|---------------|-------------------------|-------------------|------------------------|
| University of Pennsylvania Center                             | Philadelphia, PA   | 2009                | IBA           | NA                      | 5                 | 3,000                  |
| Radiation Medicine Associates & Radiation Oncology Associates | Oklahoma City, OK  | 2009                | IBA           | ProCure                 | 4                 | 1,500                  |
| Hampton University                                            | Hampton, VA        | 2010                | IBA           | NA                      | 4                 | 2,000                  |
| Siteman Cancer Center, Washington Univ.                       | St. Louis, MO      | 2008                | Still River   | NA                      | 1                 | 250                    |
| Robert Wood Johnson University Hospital                       | New Brunswick, NJ  | 2010                | Still River   | NA                      | 1                 | 250                    |
| M.D. Anderson Cancer Center                                   | Orlando, FL        | 2009                | Still River   | AMS                     | 1                 | 300                    |
| Northern Illinois University                                  | West Chicago, IL   | 2011                | TBD           | TBD                     | 4                 | 1,500                  |
| Tufts – New England Medical Center                            | Boston, MA         | 2009                | Still River   | AMS                     | 1                 | 356                    |
| Broward General Medical Center                                | Ft. Lauderdale, FL | 2010                | Still River   | NA                      | 1                 | 250                    |
| University of Oklahoma                                        | Oklahoma City, OK  | 2010                | Still River   | NA                      | 1                 | 250                    |
| Swedish Cancer Institute                                      | Seattle, WA        | 2010                | Still River   | NA                      | 1                 | 250                    |
| Radiation Oncology Consultants & Central DuPage Hospital      | West Chicago, IL   | 2010                | TBD           | ProCure                 | 4                 | 1,500                  |
| OncoLogics, Inc.                                              | Lafayette, LA      | 2011                | Still River   | NA                      | 1                 | 250                    |
| <b>Totals</b>                                                 |                    |                     |               |                         | <b>35</b>         | <b>11,256</b>          |

Three U.S. projects are currently under construction; in Philadelphia, Oklahoma City and Hampton, VA.

Eight of the projects have been announced with the intent to utilize future, still to be developed, single room technology. Projects planning to use equipment sourced by Still River Systems seem to be in a precarious position due to uncertainties related to the ongoing design, prototype, manufacturing and FDA approval process that Still River Systems has not yet completed. This may create near term business opportunities.

Combining the capacity of the five existing proton therapy centers and the announced 15 potential additional future proton therapy centers will enable the annual treatment, after 2011, of approximately 27,856 of the 258,650 local control failure patients – approximately 11% of the national target market.

We have identified 24 additional U.S. projects that are under consideration, illustrated in Table 5.

**Table 5: Potential Future U.S. Particle Therapy Projects.**



| <b>Institution</b>                       | <b>Location</b>   | <b># of Rooms</b> | <b>Annual Capacity</b> |
|------------------------------------------|-------------------|-------------------|------------------------|
| Mayo Clinic                              | Rochester, MN     | 4                 | 1,600                  |
| Mayo Clinic                              | Scottsdale, AZ    | 4                 | 1,600                  |
| University of California – San Diego     | San Diego, CA     | 4                 | 1,600                  |
| Scripps Clinic                           | San Diego, CA     | 4                 | 1,600                  |
| OnCure Medical Corporation               | Los Angeles, CA   | 1                 | 400                    |
| Touro University                         | San Francisco, CA | 4                 | 1,600                  |
| University of California – San Francisco | San Francisco, CA | 4                 | 1,600                  |
| University of California – Davis         | Davis, CA         | 1                 | 800                    |
| Seattle Cancer Care Alliance             | Seattle, WA       | 4                 | 1,600                  |
| NanoLife                                 | Denver, CO        | 4                 | 1,600                  |
| University of Texas Southwestern         | Dallas, TX        | 4                 | 1,600                  |
| NanoLife                                 | Minneapolis, MN   | 4                 | 1,600                  |
| Alexian Brothers Medical Center          | Elk Grove, IL     | 1                 | 800                    |
| Ohio State University                    | Columbus, OH      | 4                 | 1,600                  |
| St. Jude Children’s Research Hospital    | Memphis, TN       | 1                 | 800                    |
| Vanderbilt University                    | Nashville, TN     | 4                 | 1,600                  |
| Duke University                          | Durham, NC        | 4                 | 1,600                  |
| Emory University                         | Atlanta, GA       | 4                 | 1,600                  |
| OnCure Medical Corporation               | Jacksonville, FL  | 1                 | 400                    |
| Morse LLC - James G. Schwade, M.D.,      | Miami, FL         | 1                 | 800                    |
| Thomas Jefferson & Proton Therapy Inc.   | Philadelphia, PA  | 4                 | 1,600                  |
| New York Presbyterian Hospital           | New York, NY      | 4                 | 1,600                  |
| University of Pittsburgh                 | Pittsburgh, PA    | 4                 | 1,600                  |
| University of Maryland                   | College Park, MD  | 4                 | 1,600                  |
| <b>Totals</b>                            |                   | <b>78</b>         | <b>32,800</b>          |

In Table 6 identifies 36 additional projects under construction or consideration outside of the U.S. The plethora of U.S. and international projects indicates that equipment manufacturers could have a full order pipeline for many years to come.

**Table 6: Potential Global Particle Therapy Projects.**

| <b>Institution</b>                           | <b>Location</b>          | <b>Planned Open</b> | <b>Vendor</b> | <b># of Rooms</b> | <b>Annual Capacity</b> |
|----------------------------------------------|--------------------------|---------------------|---------------|-------------------|------------------------|
| Rinecker Proton Therapy Center               | Munich, Germany          | 2008                | Varian        | 5                 | 3,500                  |
| Heidelberg Ion Therapy Center                | Heidelberg, Germany      | 2008                | Siemens       | 3                 | 1,000                  |
| Paul Scherrer Institute - expansion          | Villigen, Switzerland    | 2008                | Hybrid        | 1                 | 1,000                  |
| National Center of Oncological Hadrontherapy | Pavia, Italy             | 2008                | Hybrid        | 3                 | 1,000                  |
| Universitätsklinikum Essen                   | Essen, Germany           | 2009                | IBA           | 4                 | 1,500                  |
| Rhön-Klinikum AG                             | Marburg, Germany         | 2010                | Siemens       | 4                 | 2,000                  |
| MedAustron                                   | Wiener Neustadt, Austria | 2011                | TBD           | 2                 | 1,200                  |
| Skandionkliniken                             | Uppsalla, Sweden         | 2011                | TBD           | 3                 | 1,000                  |

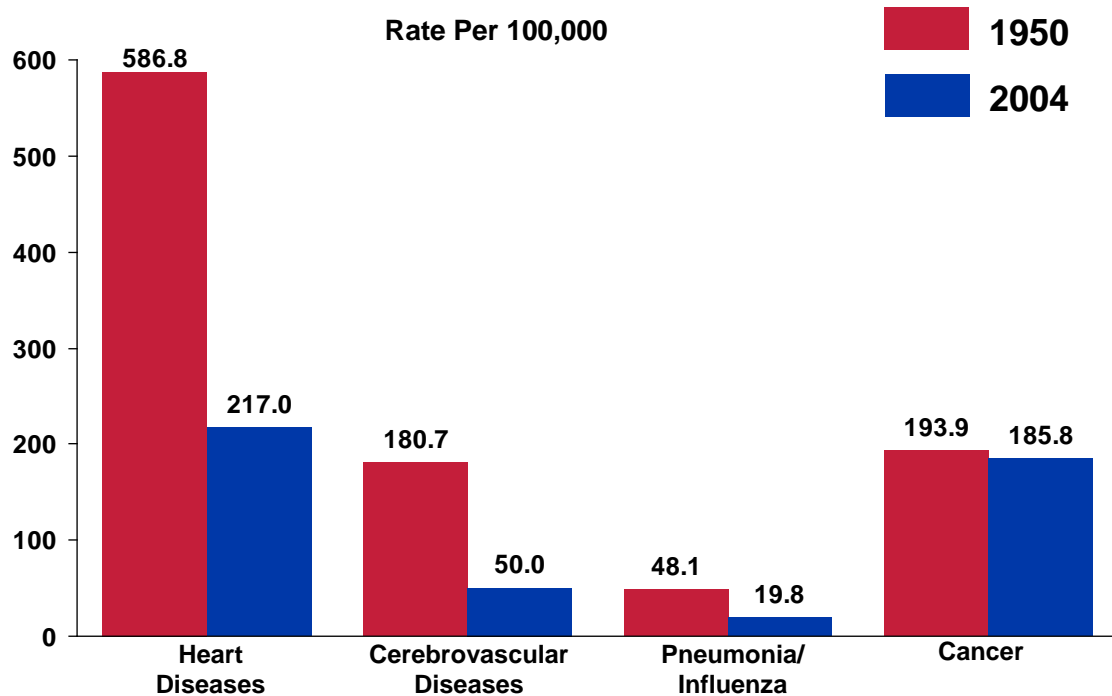
|                                                  |                             |      |        |            |               |
|--------------------------------------------------|-----------------------------|------|--------|------------|---------------|
| Universitat Klinikum Schleswig-Holstein          | Kiel, Germany               | 2012 | TBD    | 3          | 1,200         |
| Dresden University of Technology                 | Dresden, Germany            | 2012 | TBD    | 3          | 1,200         |
| Rinecker Proton Therapy Center                   | Cologne, Germany            | 2012 | TBD    | 5          | 3,500         |
| Curie Institute for Proton Therapy               | Orsay, France               | 2011 | TBD    | 3          | 1,200         |
| ETOILE – National Hadrontherapy Centre           | Lyon, France                | 2012 | TBD    | 3          | 1,200         |
| Provincial Agency for Proton Therapy             | Trento, Italy               | TBD  | TBD    | 3          | 1,200         |
| Hammersmith Hospital                             | London, England             | TBD  | TBD    | 3          | 1,200         |
| Institute for Theoretical & Experimental Physics | Moscow, Russia              | TBD  | TBD    | 4          | 1,600         |
| Petersburg Nuclear Physics Institute             | St. Petersburg, Russia      | TBD  | TBD    | 4          | 1,600         |
| Joint Institute for Nuclear Research             | Dubna, Russia               | TBD  | TBD    | 3          | 1,200         |
| Okrug Hospital                                   | Khanty-Mansiysk, Russia     | TBD  | TBD    | 2          | 800           |
| Novosibirsk State University                     | Novosibirsk, Russia         | TBD  | TBD    | 3          | 1,200         |
| Proton Therapy International                     | Istanbul, Turkey            | TBD  | TBD    | 4          | 1,600         |
| Tata Memorial Center                             | Mumbai, India               | TBD  | TBD    | 4          | 1,600         |
| Apollo Cancer Institute                          | New Delhi, India            | TBD  | TBD    | 4          | 1,600         |
| Variable Energy Cyclotron Centre                 | Kolkata, India              | TBD  | TBD    | 4          | 1,600         |
| iThemba Labs                                     | Somerset West, South Africa | TBD  | TBD    | 3          | 1,200         |
| Sino-Japanese Friendship Hospital                | Beijing, China              | 2008 | IBA    | 2          | 800           |
| Gunma University                                 | Japan                       | 2011 | Hybrid | 4          | 1,600         |
| Samsung Medical Center                           | Seoul, Korea                | TBD  | TBD    | 3          | 1,200         |
| Hyundai Hospital                                 | Seoul, Korea                | TBD  | TBD    | 3          | 1,200         |
| National Taiwan University                       | Taipei, Taiwan              | TBD  | TBD    | 3          | 1,200         |
| Chang Gung Memorial Hospital                     | Taipei, Taiwan              | TBD  | TBD    | 3          | 1,200         |
| Malaysian Institute of Nuclear Technology        | Kuala Lumpur, Malaysia      | TBD  | TBD    | 3          | 1,200         |
| National Cancer Centre                           | Singapore                   | TBD  | TBD    | 4          | 1,600         |
| Royal Prince Alfred Hosp.-Wollongong Univ.       | Sydney, Australia           | TBD  | TBD    | 4          | 1,600         |
| Austin Health–Olivia Newton-John Cancer Ctr.     | Melbourne, Australia        | TBD  | TBD    | 3          | 1,200         |
| Royal Adelaide Hospital                          | Adelaide, Australia         | TBD  | TBD    | 1          | 400           |
| <b>Totals</b>                                    |                             |      |        | <b>116</b> | <b>50,100</b> |

## Patients

As illustrated in Figure 3, innumerable advances in health care during the second half of the 20<sup>th</sup> century have made a profound impact on U.S. death rates in heart diseases, cerebrovascular diseases, pneumonia and influenza. Unfortunately, these advancements have delivered minimal change to the death rates due to cancer.

Due to population growth, the actual number of annual fatalities continues to grow. We believe that the lack of progress with regards to the cancer death rate can serve as a national “call to arms” for The Baby Boomer Generation. Once mobilized, we believe this powerful consumer group will demand access to the benefits provided by proton therapy.

**Figure 3: Change in the US Death Rates\* by Cause 1950 & 2004.**



\* Age-adjusted to 2000 US standard population.

Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.

2004 Mortality Data: US Mortality Public Use Data Tape, 2004, NCHS, Centers for Disease Control and Prevention, 2006

The advancements in cancer care that are routinely available today often induce side effects that are nearly as debilitating as the disease itself. We believe that patient fear of the commonly available treatment options exacerbates the problem of limited success in decreasing the cancer death rate. We also believe that this environment of fear and denial causes many patients to avoid readily available screening and early diagnostic methods that typically lead to early treatment and in many cases a cure.

Proton therapy is effective at treating cancer while at the same time minimizing damage to non-cancerous cells, tissues and organs. Proton therapy also provides a positive impact on the quality of life of cancer patients. We believe that the increased availability of proton therapy will have a profound impact on the mindset of cancer patients, their families and the entire health care system.

We believe that cancer patients, especially The Baby Boomer Generation, will readily embrace the benefits of particle therapy as it becomes more available. Given the characteristics of this demographic, we expect that they will be vocal proponents, demanding appropriate utilization by their physicians, and appropriate reimbursement by their government and insurance carriers.

Table 7 presents the American Cancer Society's summary of estimated new cancer cases on a State by State basis. Proton therapy, can give cancer patients a new found source of hope.

**Table 7: American Cancer Society Cancer Projections.**

### Estimated New Cancer Cases for Selected Cancer Sites by State, US, 2007\*

| State             | All Cases | Female Breast | Uterine Cervix | Colon & Rectum | Uterine Corpus | Leukemia | Lung & Bronchus | Melanoma of the Skin | Non-Hodgkin Lymphoma | Prostate | Urinary Bladder |
|-------------------|-----------|---------------|----------------|----------------|----------------|----------|-----------------|----------------------|----------------------|----------|-----------------|
| Alabama           | 20,590    | 2,750         | 170            | 2,350          | 460            | 550      | 3,850           | 740                  | 860                  | 3,010    | 850             |
| Alaska            | 2,500     | 340           | †              | 270            | 60             | 70       | 330             | 80                   | 110                  | 420      | 110             |
| Arizona           | 26,270    | 3,220         | 190            | 2,750          | 550            | 740      | 3,740           | 1,300                | 1,080                | 3,400    | 1,360           |
| Arkansas          | 14,130    | 1,830         | 130            | 1,640          | 320            | 510      | 2,420           | 550                  | 600                  | 1,960    | 560             |
| California        | 151,250   | 19,790        | 1,350          | 15,000         | 3,870          | 4,610    | 17,920          | 6,860                | 7,190                | 24,590   | 6,590           |
| Colorado          | 19,190    | 2,660         | 150            | 1,790          | 490            | 670      | 2,100           | 1,210                | 880                  | 3,160    | 880             |
| Connecticut       | 19,780    | 2,510         | 100            | 2,190          | 650            | 610      | 2,720           | 1,120                | 870                  | 2,890    | 1,090           |
| Delaware          | 4,530     | 560           | †              | 480            | 130            | 110      | 770             | 190                  | 170                  | 800      | 220             |
| Dist. of Columbia | 2,540     | 320           | †              | 270            | 70             | 60       | 380             | 60                   | 100                  | 540      | 90              |
| Florida           | 106,560   | 11,710        | 850            | 11,420         | 2,490          | 3,360    | 17,490          | 4,380                | 4,530                | 15,710   | 5,460           |
| Georgia           | 35,440    | 4,520         | 330            | 3,690          | 810            | 960      | 5,780           | 1,460                | 1,370                | 5,850    | 1,360           |
| Hawaii            | 6,020     | 820           | 50             | 790            | 170            | 170      | 690             | 270                  | 250                  | 780      | 200             |
| Idaho             | 6,140     | 780           | †              | 600            | 150            | 220      | 760             | 350                  | 280                  | 1,080    | 310             |
| Illinois          | 62,010    | 7,030         | 530            | 6,890          | 1,730          | 2,030    | 9,550           | 2,050                | 2,670                | 8,060    | 2,880           |
| Indiana           | 30,040    | 3,560         | 240            | 3,390          | 880            | 910      | 5,210           | 1,220                | 1,310                | 3,710    | 1,390           |
| Iowa              | 16,540    | 2,000         | 100            | 1,930          | 500            | 620      | 2,290           | 690                  | 800                  | 2,140    | 820             |
| Kansas            | 12,760    | 1,750         | 100            | 1,360          | 360            | 420      | 1,870           | 430                  | 600                  | 1,490    | 570             |
| Kentucky          | 22,850    | 2,590         | 200            | 2,570          | 560            | 680      | 4,450           | 1,050                | 900                  | 2,880    | 970             |
| Louisiana         | 22,540    | 2,820         | 200            | 2,520          | 420            | 680      | 3,510           | 670                  | 920                  | 3,640    | 850             |
| Maine             | 8,340     | 980           | †              | 880            | 270            | 250      | 1,360           | 410                  | 330                  | 1,210    | 470             |
| Maryland          | 26,390    | 3,560         | 190            | 2,870          | 810            | 630      | 4,130           | 1,150                | 1,160                | 4,690    | 1,150           |
| Massachusetts     | 34,920    | 4,260         | 180            | 3,850          | 1,110          | 1,010    | 5,060           | 1,820                | 1,550                | 5,180    | 1,950           |
| Michigan          | 54,410    | 5,900         | 370            | 5,570          | 1,610          | 1,680    | 8,210           | 2,080                | 2,250                | 8,200    | 2,700           |
| Minnesota         | 25,420    | 3,240         | 150            | 2,650          | 750            | 920      | 3,160           | 1,130                | 1,170                | 4,800    | 1,250           |
| Mississippi       | 12,470    | 1,620         | 120            | 1,440          | 230            | 340      | 2,190           | 320                  | 480                  | 2,010    | 480             |
| Missouri          | 29,930    | 3,730         | 240            | 3,380          | 830            | 890      | 5,350           | 870                  | 1,260                | 3,910    | 1,350           |
| Montana           | 4,920     | 630           | †              | 520            | 120            | 170      | 690             | 190                  | 220                  | 940      | 260             |
| Nebraska          | 8,720     | 1,160         | 60             | 920            | 260            | 290      | 1,190           | 340                  | 400                  | 1,260    | 430             |
| Nevada            | 11,030    | 1,180         | 80             | 1,120          | 230            | 330      | 1,750           | 390                  | 420                  | 1,550    | 570             |
| New Hampshire     | 7,140     | 890           | †              | 800            | 230            | 190      | 1,010           | 370                  | 290                  | 1,050    | 390             |
| New Jersey        | 49,370    | 6,080         | 350            | 5,160          | 1,550          | 1,520    | 6,310           | 2,210                | 2,200                | 8,070    | 2,450           |
| New Mexico        | 8,030     | 1,080         | 70             | 790            | 200            | 310      | 940             | 420                  | 350                  | 1,410    | 350             |
| New York          | 100,960   | 12,580        | 790            | 10,710         | 3,240          | 3,080    | 13,390          | 3,070                | 4,540                | 15,770   | 4,980           |
| North Carolina    | 38,210    | 4,870         | 280            | 4,290          | 1,020          | 1,070    | 6,290           | 1,630                | 1,610                | 6,040    | 1,690           |
| North Dakota      | 3,340     | 440           | †              | 410            | 100            | 110      | 390             | 120                  | 150                  | 520      | 200             |
| Ohio              | 59,220    | 6,710         | 390            | 6,410          | 1,800          | 1,710    | 9,790           | 2,390                | 2,560                | 8,260    | 2,940           |
| Oklahoma          | 17,170    | 2,200         | 160            | 1,880          | 400            | 570      | 3,180           | 720                  | 770                  | 2,510    | 710             |
| Oregon            | 18,630    | 2,460         | 110            | 1,830          | 470            | 500      | 2,520           | 990                  | 890                  | 2,870    | 970             |
| Pennsylvania      | 75,130    | 8,860         | 420            | 8,220          | 2,400          | 2,240    | 10,500          | 3,120                | 3,330                | 12,230   | 4,030           |
| Rhode Island      | 6,360     | 730           | †              | 690            | 190            | 170      | 920             | 300                  | 260                  | 920      | 370             |
| South Carolina    | 21,370    | 2,600         | 190            | 2,230          | 480            | 550      | 3,460           | 870                  | 780                  | 3,380    | 840             |
| South Dakota      | 3,990     | 510           | †              | 470            | 120            | 130      | 490             | 160                  | 180                  | 710      | 220             |
| Tennessee         | 28,440    | 3,690         | 250            | 3,100          | 660            | 800      | 5,110           | 980                  | 1,180                | 3,000    | 1,230           |
| Texas             | 91,020    | 12,120        | 940            | 9,510          | 2,040          | 3,130    | 13,520          | 3,860                | 4,140                | 13,280   | 3,300           |
| Utah              | 7,660     | 920           | 50             | 740            | 220            | 300      | 600             | 500                  | 380                  | 1,510    | 340             |
| Vermont           | 3,500     | 420           | †              | 390            | 110            | 80       | 440             | 150                  | 140                  | 550      | 170             |
| Virginia          | 35,090    | 4,570         | 280            | 3,530          | 970            | 900      | 5,360           | 1,510                | 1,390                | 5,330    | 1,380           |
| Washington        | 31,080    | 4,090         | 150            | 2,920          | 800            | 960      | 3,970           | 1,630                | 1,500                | 5,000    | 1,490           |
| West Virginia     | 10,490    | 1,180         | 80             | 1,210          | 310            | 300      | 2,110           | 410                  | 430                  | 1,430    | 500             |
| Wisconsin         | 28,130    | 3,340         | 170            | 3,090          | 860            | 1,040    | 3,930           | 1,070                | 1,300                | 4,770    | 1,350           |
| Wyoming           | 2,340     | 310           | †              | 260            | 60             | 70       | 290             | 100                  | 110                  | 410      | 110             |
| United States     | 1,444,920 | 178,480       | 11,150         | 153,760        | 39,080         | 44,240   | 213,380         | 59,940               | 63,190               | 218,890  | 67,160          |

\*Rounded to nearest 10. Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. †Estimate is fewer than 50 cases.

**Note:** These estimates are offered as a rough guide and should be interpreted with caution. State estimates may not add up to US total due to rounding and exclusion of state estimates fewer than 50 cases.

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## Conventional Treatment Technologies

Many highly effective treatment methods have been developed to combat cancer. While particle therapy could be used in lieu of conventional treatment methods in many cases, it will serve as a complementary, non-competitive tool for the foreseeable future. Due to severe limitations in the availability of particle therapy, we believe that the primary application for particle therapy is to treat the patient group that is subject to local control failure – this patient group amounts to approximately 18% of all cancer patients.

**RT** – Radiation therapy, also known as external beam therapy (EBT) is the generic terminology for a method for delivering a beam of high-energy x-rays or cobalt-60 gamma rays – photons – to the location of the patient's tumor. The beam is generated outside the patient, usually by a linear accelerator, and is targeted at the tumor site. These x-rays can destroy the cancer cells, but despite careful treatment planning, the surrounding normal tissues also receive significant radiation creating significant side effects due to the inevitable damage to normal tissue. Proton beam therapy has inherent advantages over conventional external beam radiation therapy due to the laws of physics and the resultant Bragg peak effect of particles.

**IMRT** – Intensity Modulated Radiotherapy, IMRT, is the generic terminology for enhanced delivery methods for external beam radiation therapy. IMRT provides precision enhancements relative to standard external beam radiotherapy treatments. Rather than having a single large radiation beam pass through the body, with IMRT the radiation is effectively broken up into a number radiation beams. With millimeter accuracy, these beams enter the body from many angles and intersect on the cancer. This results in a higher dosage to the tumor and a lower dose to the surrounding healthy tissues. While IMRT provides a significant improvement in delivery methodology to conventional radiation therapy, IMRT is also based on the delivery of photons and retains the shortcomings of conventional radiation therapy. IMRT does not incorporate the Bragg Peak advantages provided by particle therapy. IMRT type delivery enhancements are applicable to the delivery of particle therapy – IMPT – Intensity Modulated Proton (Particle) Therapy.

**IGRT** – Image Guided Radiotherapy, IGRT, is the generic terminology used to describe the recently developed technological approach of integrating planar x-ray or volumetric x-ray imaging into the IMRT treatment device. This enables the adjustment of the radiation beam relative to the tumor and critical organs, while the patient is in the treatment position. IGRT enhancements are applicable to the delivery of particle therapy.

**Stereotactic radiosurgery** – Stereotactic radiosurgery is the generic terminology for a form of external beam radiation therapy that has been used for more than 30 years for the non-invasive treatment of benign and malignant tumors, vascular malformations, and other disorders of the brain. Radiosurgery involves delivering high doses of focused radiation to a specific area in the body. Target location is determined stereotactically — through the use of a reference system in 3-D space. To determine the 3-D coordinates, an imaging study such as a CT or MRI scan is obtained and compared to the actual anatomy.

**Gamma Knife®** – Gamma Knife is the trade name for a stereotactic radiosurgery instrument used to treat arteriovenous malfunctions (AVM) and certain brain tumors without an incision. The Gamma Knife uses Cobalt-60 to deliver 201 beams of radiation intersecting at the target area. The risk of complications, as compared to open surgery, is less and it is a gentler form of treatment for the patient. Gamma Knife surgery can normally be performed in a day, and the convalescence time is extremely short. Gamma Knife surgery is limited to applications in the brain and is subject to the inherent limitations of photon based external beam radiation therapy.

**CyberKnife®** – CyberKnife is the trade name for a stereotactic radiosurgery instrument. Incorporating a compact, lightweight linear accelerator mounted on a robotic arm, the CyberKnife provides the surgeon high flexibility in targeting. Advanced image guidance technology tracks patient and target position

during treatment, ensuring accuracy without the use of an invasive head frame. The CyberKnife with DTS (Dynamic Tracking Software) is cleared to provide radiosurgery for lesions anywhere in the body when radiation treatment is indicated. The CyberKnife has often been used to radiosurgically treat otherwise untreatable tumors and malformations. Moreover, this instrument treats tumors at body sites, most of which are unreachable by other stereotactic systems. While the CyberKnife is an advanced method of stereotactic radiosurgery, it is subject to the inherent limitations of photon based external beam radiation therapy.

**TomoTherapy®** – TomoTherapy is a niche player in the radiotherapy marketplace. *Hi-Art®* is the trade name for their radiotherapy system combining IMRT with an integrated helical CT imaging system and spiral delivery pattern to deliver the radiation treatment. Photon radiation is produced by a linear accelerator, which travels in multiple circles all the way around the gantry ring. The accelerator moves in unison with a device called a multi-leaf collimator, or MLC. The computer-controlled MLC has two sets of interlaced leaves that move in and out very quickly to constantly modulate the radiation beam as it leaves the accelerator. Meanwhile, the couch is also moving, guiding the patient slowly through the center of the ring, so each time the accelerator rotates the patient it is directing the beam at a slightly different plane. While TomoTherapy is an advanced form of IMRT, it is subject to the inherent limitations of photon based external beam radiation therapy. Recognizing this, TomoTherapy entered into a license agreement with Lawrence Livermore National Laboratory for the development of a proton therapy product. TomoTherapy expects that it will be 5 years before clinical trials can begin.

**Brachytherapy** – Brachytherapy is an advanced cancer treatment. Radioactive seeds or sources are placed in or near the tumor itself, giving a high radiation dose to the tumor while reducing the radiation exposure in the surrounding healthy tissues. The term "brachy" is Greek for short distance, and brachytherapy is radiation therapy given at a short distance: localized, precise, and high-tech.

There are two methods of brachytherapy, HDR (high dose rate) and permanent or low dose rate implants. There are also two kinds of HDR. Interstitial brachytherapy HDR usually employs a Cs-137 source. Indwelling catheters, about a half inch internal diameter are inserted to the distal boundary of the tumors. A radioactive source is then positioned at the end of the catheter and allowed to remain for a specified time period (dwell time) to deliver the required dose. It is then withdrawn certain distance and allowed to dwell again. The process is repeated multiple times, depending on the area to be covered. Frequently, there are multiple catheters inserted. The average breast HDR is usually 3-4 tubes. The open catheters (sometimes called cannulae) are left in the patient for 18-36 hours as multiple treatments every 6-12 hours are required to deliver the desired total dose. This method is painful and a true inconvenience for the patient. Intracavitary brachytherapy is employed for body openings. If the opening is the cervix or uterus, a surgical procedure is required to insert a template which is used to guide the HDR source. Throat, rectum, nose and vaginal openings are treated with intracavitary brachytherapy in this manner.

Permanent implants are used in the prostate and also in the breast and only recently in gynecological lesions. With this approach, rice sized (0.5 x 4.5 mm) radioactive seeds are permanently inserted into the target area, usually by means of a long (10") needle. The prostate is about 60cc in size (about the size of a walnut). These seeds are either I-131 (60 day T1/2) or Pd-103 (16 day T1/2) depending on whether fast or slow dose delivery is desired. About 100 seeds are used in each prostate. Each needle delivers 4-7 seeds and an equal number of spacers.

Pain, discomfort and some dose inaccuracies are the disadvantage for HDR, plus time in the hospital and recovery time. There is risk of infection as well. Seeds are subject to migration. The prostate has the texture of a peeled avocado. If they migrate into the ureter or seminal vesicles they can be ejected from



the body. If they do not migrate, they can rotate in place, skewing the dose distribution by a factor of 9 (0.5-4.5). Also, neither seed work is indicated for patients with an elevated Gleason score.

**Cryosurgery** – Cryosurgery, also called cryotherapy, is the use of extreme cold produced by liquid nitrogen (or argon gas) to destroy abnormal tissue. When used to treat external tumors, liquid nitrogen is applied directly to the cancer cells with a cotton swab or spraying device. When used to treat internal tumors, liquid nitrogen or argon gas is circulated through a hollow instrument called a cryoprobe, which is placed in contact with the tumor. The doctor uses ultrasound or MRI to guide the cryoprobe and monitor the freezing of the cells, thus limiting damage to nearby healthy tissue. A ball of ice crystals forms around the probe, freezing nearby cells. Sometimes more than one probe is used to deliver the liquid nitrogen to various parts of the tumor. The probes may be put into the tumor during surgery or through the skin (percutaneously). After cryosurgery, the frozen tissue thaws and is either naturally absorbed by the body (for internal tumors), or it dissolves and forms a scab (for external tumors). The major disadvantage of cryosurgery is the uncertainty surrounding its long-term effectiveness. While cryosurgery may be effective in treating tumors the physician can see by using diagnostic imaging tests, it can miss microscopic cancer spread. Furthermore, because the effectiveness of the technique is still being assessed, insurance coverage issues may arise.

**Sono ablation** – Sono ablation is a therapeutic device developed by InSightec, Inc., that ablates soft tissue, using thermal energy generated with high intensity focused ultrasound, guided by Magnetic Resonance Imaging (MRI). The ultrasound is focused in a manner similar to how a magnifying glass focuses light. The ultrasound waves are directed from a transducer (a device that converts electrical energy into ultrasound energy) into a small focal volume. During treatment, the beam of focused ultrasound energy penetrates through soft tissue and produces well defined regions of protein denaturation, irreversible cell damage, and coagulative necrosis, at specific target locations. A single exposure of focused ultrasound energy is called a “sonication.” Multiple sonications are necessary to ablate the targeted tissue. Tight focusing is designed to limit the ablation to the targeted location. This system has been approved by the FDA for the treatment of fibroids only, although the company is investigating other applications.

**Hyperthermia** – This therapeutic approach employs local organ or lesion heating by focused radiofrequency, either broadcast (if superficial enough) or through an indwelling RF catheter (antenna) if deeper. There are two major equipment vendors, Varian, through the 1992 acquisition of Texas based Clinitherm, and BSD of Salt Lake City. Hyperthermia is used infrequently as a stand alone therapeutic modality. It has been shown to be a good adjuvant therapy, usually coupled with external beam photon therapy. Heating tissue to 6-8 degrees C above normal will impede the cells ability to reproduce, and over time will kill them. Hyperthermia is also a radiation sensitizer, rendering tumorous cells less resistant to radiation. We anticipate that this modality could add clinical support to proton therapy.

**Anti-protons** – The use of anti-protons, or anti-matter, is currently in the investigational stage. Initial indications are that anti-protons would be even more effective at killing cancer cells than protons, however many obstacles must be overcome before this can become a viable clinical method. Should anti-proton technology mature to the point of commercialization, in theory the technology could be incorporated into existing proton therapy facilities, enhancing patient throughput.

**Laser generated protons and particles** – Research is being conducted to explore methods to use high powered lasers to generate therapeutic particles. Researchers have successfully used high powered lasers to pulse a target foil thereby generating a broad energy spectrum of protons and ions. However accelerator physicists expect that it will be at least twenty years until laser generated proton therapy will become a clinical tool. Work that needs to be done includes the development of high power lasers to enable the generation of protons and ions with therapeutic energies, improvements in target foil design to

enable the foil to survive beyond a single laser pulse and proton beam energy and shape selection systems.

**Gene Therapy, Molecular Medicine, and other “silver bullets”** – A myriad array of promising methods to treat cancer in novel, non-invasive and customized manners, however, by and large they are investigational at best. It will take many years of research, development and validation before one becomes a mainstream, reimbursed treatment option.

## **The Product – Particle Therapy**

Cancer is widely recognized as a debilitating disease. Oftentimes, the therapy that cancer patients must endure is just as debilitating as the disease itself. Surgery has its obvious risks. Chemotherapy is a systemic treatment that wreaks havoc on the patient’s body in an effort to stem the growth of cancerous cells. Conventional x-radiation therapy, while providing a more localized treatment, still causes significant damage to surrounding tissues and organs.

Particle therapy is a specialized tool for the delivery of ionizing radiation for cancer patients. While treating cancer is currently the primary use for particle therapy, additional uses include the treatment of certain physical malformations such as arteriovenous malformations and macular degeneration.

Pediatric cancer patients are especially sensitive to the negative effects of conventional radiation therapy – growth abnormalities, secondary malignancies, neurologic complications, cardiac and pulmonary toxicities and infertility can be avoided by using proton therapy.

## **Technology Overview**

Protons, electrons and neutrons are the basic building blocks of atoms. Physicists began using particles over fifty years ago to treat cancer through the use of specialized particle accelerators – cyclotrons and synchrotrons. These accelerators use sophisticated magnets to accelerate particles to near the speed of light. Through this acceleration process a substantial amount of energy is imparted to the particles. Additional magnets, control systems and delivery systems then direct the particles with sub-millimeter accuracy to deposit their energy within the cancerous tissues, causing catastrophic damage to the DNA of the cancerous cells.

This damage results in cell death or the inability to replicate. Because this damage can be confined to the cancerous tissues, damage to healthy tissues and organs surrounding the cancer is minimized. Patients undergoing treatment with particles benefit from a decreased level of side effects when compared to conventional radiation therapy. Since particles provide a proven method to combat cancer while simultaneously minimizing side effects, particle therapy provides cancer patients with a source of hope.

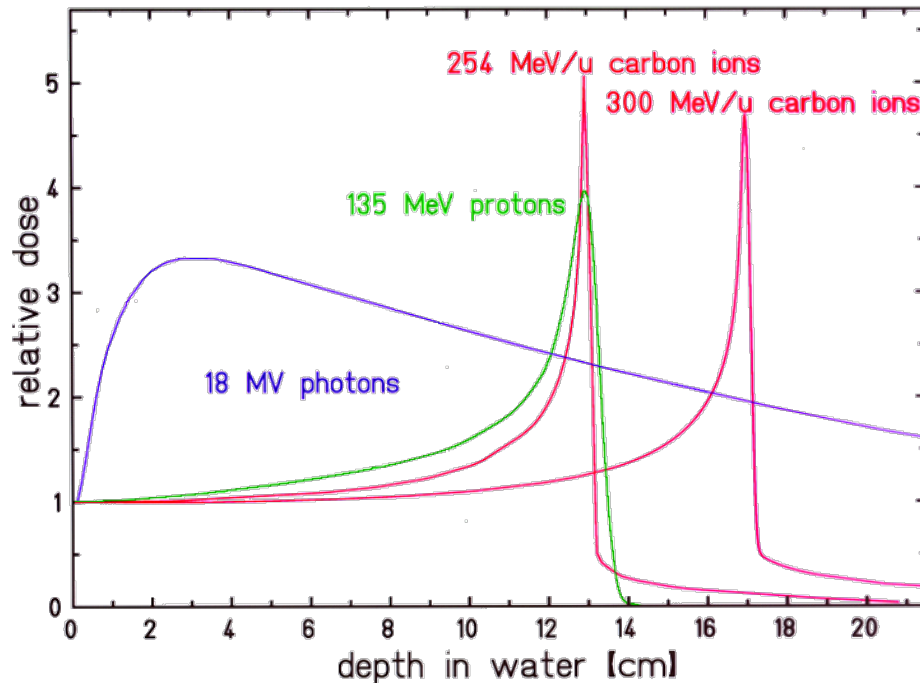
In 1946 Robert Wilson, PhD, a veteran of the nuclear weapons development program during World War II, first proposed that protons be used for cancer therapy. Wilson recognized that the physical properties of protons made them ideal for therapeutic use. Protons and other therapeutic particles such as carbon, oxygen and helium have a much higher mass than photons, limiting the effects of scatter as they pass through a patient’s body. More importantly, unlike photons, the absorbed energy of a particle beam increases gradually as it penetrates the patient’s body and rises to a peak at the end of its range. This effect was first described by William Henry Bragg, PhD, a British physicist in 1903 and is commonly known as the Bragg Peak.

This unique characteristic allows physicians to precisely deposit the maximum energy dose within the tumor volume – the location of the Bragg Peak is variable providing physicians with unprecedented control. The depth of the Bragg Peak is varied by adjusting the amount of energy – the speed – that the



particles have when they enter the patient's body. As illustrated in Figure 5, the energy deposition immediately beyond the Bragg Peak is essentially zero, sparing normal tissues beyond the tumor itself. Also note that the energy deposition before the Bragg Peak is substantially lower than conventional photon radiation therapy.

**Figure 5: Depth dose distribution of various radiotherapies.**



Ironically, the precise nature of particle therapy has served to impede its adoption for nearly 50 years. Taking advantage of the precision of proton therapy requires an equally precise method of medical imaging and beam control. Fortunately, computer technology has advanced during the past decade to enable the widespread utilization of high resolution Computed Tomography (“CT”) Magnetic Resonance Imaging (“MRI”) and Positron Emission Tomography (“PET”).

The medical industry has now progressed to the point that Wilson’s vision is becoming a reality. Proton therapy is a reimbursed, advanced form of radiation therapy ideally suited for the precise treatment of a wide variety of cancers that have been diagnosed at early stages. Like other radiotherapy methods, proton therapy offers excellent clinical outcomes; however, proton therapy causes far fewer side effects. Despite its benefits, there are only five clinically based facilities performing proton beam therapy on a regular basis in the U.S.

As demonstrated in Figure 6, conventional radiation therapy deposits energy throughout its path through the patient’s body causing extensive damage to healthy tissue and organs; in this case the heart, lungs and spine. This additional radiation typically results in debilitating side effects. The energy is highest at the point of entrance and decreases as it passes through the patient’s body.

**Figure 6: X-rays enter patient (at the arrows) & pass through the patient.**



This deposition of energy causes the ionization of atoms resulting in subsequent changes in molecular and DNA structures. These changes ultimately lead to cell death and the control of cancerous growths. The challenge is to ensure that cancerous cells receive an adequate dose of energy while sparing normal cells.

Figure 7 illustrates how particle therapy overcomes the limitations of conventional radiation therapy by stopping in the tumor, thereby taking advantage of the Bragg Peak, depositing cancer killing energy where it provides the most benefit.

**Figure 7: Particles enter patient (at the arrows) and stop in the tumor.**



An additional benefit of the Bragg Peak effect is that it aids clinicians in their effort to maintain compliance with guidelines dictating the need for minimal radiation exposure to healthy tissue.

Heavier particles may provide several distinct advantages over protons. A prime benefit of heavy particles such as carbon ions, is that they have a greater relative biological effect (RBE). By nature of their greater RBE, carbon ions deposit more energy when they reach their Bragg Peak – more energy translates into more killing power. An additional benefit is that heavy particles are more massive – more mass translates into less scattering of the particles, resulting in more precise placement. A third advantage of carbon ions is the ability to integrate PET imaging into the therapy delivery process, thus providing physicians with in vivo verification of dose delivery for the first time.

Due to their enhanced RBE characteristics, extensive research with carbon ions has been performed in Japan to explore the possibility of decreasing the number of fractions required to treat cancer. Good results have been demonstrated in decreasing the number of fractions from 20+ fractions to a single fraction. Non-related physicians have stated that the published results for treating patients with inoperable lung cancer are comparable to the results for surgical candidates. While treatment with heavier particles appears promising, the long term effects of enhanced RBE require further study.

Cancer therapy with helium, oxygen and carbon ions is not reimbursed at this time. The reimbursement case will be built on the combined benefits of improved outcomes, decreased side effects and lower cost to the health care system. Today, there are three locations where carbon ion therapy is being performed – two in Japan and one in Germany.

### **Particle Therapy – The Process**

Like other methods for the delivery of external beam radiation therapy, proton therapy entails the delivery of a total therapeutic dose in a daily series of small doses called fractions which are applied over the course of several weeks. This process is called fractionation. The number of fractions is variable and is determined by the type of cancer being treated and its location in the patient's body. The number of fractions ranges from less than 10 to over 40. Each fraction entails the delivery of the prescribed dosage of particles over a period of a few seconds to 2-3 minutes. This is a multifaceted process which is provided by a team of highly skilled care givers.

Upon diagnosis with cancer, the patient is generally referred to an Oncologist. The Oncologist determines the appropriate course of treatment for the patient after a thorough diagnostic work up. Options typically include surgery, radiation therapy and chemo therapy or possibly a combination of the three.

When radiation therapy is deemed appropriate, the patient is referred to a Radiation Oncologist. The Radiation Oncologist reviews the patient's diagnostic workup, orders additional tests as required and prescribes the appropriate dosage and delivery method – proton therapy versus conventional radiation therapy.

A Medical Physicist reviews the prescribed dosage and works with a Dosimetrist to develop a patient specific treatment plan utilizing specialized software tools. Once the treatment plan is agreed to by the Radiation Oncologist, Medical Physicist and Dosimetrist the plan is handed off to a Radiation Therapist who is responsible for configuring the proton therapy system and delivering the radiation dosage per the treatment plan. The treatment plan normally calls for the inclusion of patient specific, reusable specialized devices – treatment aids and immobilization devices or molds. The Radiation Therapist typically is assisted in delivering proton therapy by Radiation Therapy Assistants, Immobilization Technicians and Mold Technicians. Radiation Therapy Assistants are responsible for escorting the patient

to the treatment room, correctly positioning the patient and interacting with the patient. Immobilization Technicians are responsible for applying immobilization devices to the patient and interacting with the patient. Mold Technicians are responsible for the fabrication of immobilization devices and molds.

Nurses are also on the premises in the event of emergency care requirements and to answer patient's medical questions. During the course of the treatment additional CT scans are typically performed weekly to allow the plan to be adjusted as necessary. Daily x-ray imaging is performed to insure accurate delivery of the radiation dose. PET imaging is becoming a routine component of the planning, treatment and follow up process..

### **Transition to Commercial Opportunity – Technology Vendors**

During the 1990's, proton therapy began its transition from the realm of research institutions to clinical institutions with the construction of the world's first hospital based proton therapy facility located at Loma Linda University Medical Center in southern California.

This transition has inspired several companies to make substantial investments to design and market commercial proton therapy systems. Proton therapy equipment utilized in the U.S. must receive clearance by the Food and Drug Administration ("FDA") prior to clinical use and reimbursement.

Historically, proton therapy equipment solutions have been designed to use one accelerator, a cyclotron or synchrotron, to accelerate particles which are directed to multiple treatment rooms via a beam line outfitted with focusing and switching magnets, ostensibly to spread the capital cost of the accelerator over multiple treatment rooms. Today's commercially available products are based on this multi-room design philosophy.

Three vendors, Still River Systems, Accel and TomoTherapy, have recently introduced proton therapy design solutions that incorporate superconducting synchrocyclotrons. This design approach offers the promise of a smaller, lower cost accelerator that could enable the manufacture of single room solutions. While Still River Systems has accepted orders for several systems, we are aware that it has not yet built a working system nor has it secured FDA clearance. Varian Medical Systems, a leading radiation therapy company, completed its acquisition of Accel in January of 2007. Varian has not announced its intentions regarding the commercialization of the Accel single room design.

We have engaged in an extensive evaluation of particle therapy technology and the companies marketing the technology. Worldwide, there are seven companies presenting particle solutions as indicated in Table 8. Additional information about each of these companies is provided in "The Product – Particle Therapy" section of this document.

**Table 8: Companies marketing particle therapy solutions.**

| <b>Vendor</b>               | <b>U.S. Market</b> | <b>FDA Clearance</b> | <b>Single-room</b> | <b>Multi-room</b> | <b>Heavy Particles</b> |
|-----------------------------|--------------------|----------------------|--------------------|-------------------|------------------------|
| Hitachi                     | Yes                | Yes                  | No                 | Yes               | No                     |
| Ion Beam Applications (IBA) | Yes                | Yes                  | No                 | Yes               | Yes                    |
| Mitsubishi                  | No                 | No                   | No                 | Yes               | ?                      |
| Optivus                     | Yes                | Yes                  | No                 | Yes               | No                     |
| Siemens Medical Systems     | Yes                | No                   | No                 | Yes               | Yes                    |
| Still River Systems         | Yes                | No                   | Yes                | No                | No                     |

|                        |     |    |     |     |    |
|------------------------|-----|----|-----|-----|----|
| TomoTherapy            | Yes | No | Yes | No  | No |
| Varian Medical Systems | Yes | No | No  | Yes | No |

Pricing information obtained indicates that there is no appreciable per room price differential between multi-room designs and single room designs. The primary benefit appears to be that the single room approach could lower the barrier of entry for proton therapy to \$20-25M.

**Hitachi** – <http://www.hitachi.us/>

Hitachi, a multi national technology company established in 1910, claims a “corporate philosophy of contributing to society through technology”. In recent years this has been demonstrated by its participation in commercial proton therapy design and manufacturing. Three proton therapy facilities in Japan currently utilize Hitachi equipment. Hitachi has recently installed its first U.S. system, which is located at M.D. Anderson Cancer Center in Houston, Texas. Hitachi received FDA clearance in March of 2006. The first patient treatment occurred at M.D. Anderson in May of 2006.

**IBA** – <http://www.iba-worldwide.com/healthcare/radiotherapy/particle-therapy/>

IBA, Ion Beam Applications is based in Belgium. IBA has been actively involved in proton therapy beginning with its first system located at the National Cancer Center in Kashiwa, Japan which has been treating patients since 1998. IBA has secured FDA approval for their initial system located at Massachusetts General Hospital. IBA has been successful in securing additional contracts for new projects around the world, including the recently completed facility in Jacksonville, Florida for the University of Florida, Hampton University in Hampton Roads, Virginia, The University of Pennsylvania, in Philadelphia, Pennsylvania, Essen University in Essen, Germany and a private center under development in Oklahoma City, Oklahoma. IBA is the market share leader and should be considered as one of the technological leaders in proton therapy.

**Mitsubishi** – [http://global.mitsubishielectric.com/bu/particlebeam/index\\_b.html](http://global.mitsubishielectric.com/bu/particlebeam/index_b.html)

Mitsubishi Electric, a global leader in the manufacture, marketing and sales of electrical and electronic equipment for home products, commercial and industrial systems and equipment products was founded over 80 years ago. Mitsubishi has supplied the equipment for two proton therapy facilities, both of which are located in Japan. The Hyogo Ion Beam Medical Center became operational in 2001. Mitsubishi does not market its product in the U.S. at this time; this may be related to past FDA recalls of Mitsubishi radiation therapy equipment.

**Optivus Technology, Inc.** – <http://www.optivus.com/>

Optivus, a company based in San Bernardino, California, is a direct result of the joint public-private project that created the proton beam therapy facility at Loma Linda. The system marketed by Optivus has the advantage of clinical validation provided by the thousands of patients that have been treated at Loma Linda. Further, Optivus has secured FDA approval for their system. To the Company’s knowledge, Optivus has not secured contracts for any new system installations.

**Siemens** – <http://www.siemens.com/>

Siemens, founded over 150 years ago, is a global company that specializes in electrical engineering and electronics. Siemens is active in the areas of Information and Communications, Automation and Control, Power, Transportation, Medical, and Lighting. Siemens has recently entered the particle therapy market by virtue of licensing agreements with the University Clinic Heidelberg, the German Cancer Research Center (DKFZ), the Gesellschaft für Schwerionenforschung (GSI) and the Research Center Rossendorf (FZR). Siemens is a participant in the process of installing a combined proton + particle therapy system at the University Clinic in Heidelberg, Germany. Siemens has secured its first solo order for a system from Rhön-Klinikum AG which will be installed at the Geissen/Marburg University Hospital. Siemens will integrate an accelerator sourced from Danish firm Danfysik for the Marburg and subsequent projects. The

product offered by Siemens is designed to deliver all particles, protons through carbon ions. This design approach does not permit a proton only configuration, making it cost prohibitive and eliminating Siemens from consideration for most projects.

**Still River Systems** – <http://www.stillriversystems.com/>

Still River Systems is a development stage company based in Littleton, Massachusetts that is working to develop a single room proton therapy solution. Still River Systems was formed in early 2004 receiving \$425K in seed funding from Varian Medical Systems. This was followed by Series A round raising \$4.7M in Q1 2005, Series B round raising \$8M in Q2 2006 and Series C round raising \$6.8M in Q4 2007. Still River Systems' goal is to deliver its first system in 2008. When completed, the Still River Systems product will not be capable of treating with heavier particles such as helium, oxygen or carbon ions. To our knowledge, Still River Systems has not assembled a prototype system and has not secured FDA. Despite the uncertainties surrounding its product Still River Systems has secured orders for 8 systems.

**TomoTherapy, Inc.** – <http://www.tomotherapy.com/>

TomoTherapy was founded in 1997. Headquartered in Madison, Wisconsin, TomoTherapy markets a niche radiation therapy device developed at the University of Wisconsin. TomoTherapy's device integrates conventional IMRT technology with an onboard CT imaging device. TomoTherapy began shipping product in 2003 and has installed over 150 systems worldwide. TomoTherapy completed its initial public offering in May 2007, raising approximately \$186M on the NASDAQ Global Market. Recognizing the inherent limitations in conventional IMRT TomoTherapy announced its intention to enter the proton therapy business via a collaboration with Lawrence Livermore National Laboratory. TomoTherapy is concentrating on the market for single room proton therapy devices. Co-founder Rock Mackie, PhD has stated that "clinical trials of their system are at least five years away".

**Varian Medical Systems** – <http://www.varian.com/> <http://www.accel-instruments.net/>

Varian Medical Systems is a leader in the design and manufacture of equipment and software for treating cancer with radiation therapy and neurological conditions with radiosurgery. The company is also a leading supplier of x-ray tubes and flat-panel digital technology for imaging in medical, scientific and industrial applications. In January of 2007, Varian Medical Systems entered the proton therapy equipment arena by nature of its acquisition of Accel Instruments GmbH. Accel was a small German engineering and manufacturing company specializing in custom designed research and industrial equipment. Accel has experience with RF accelerating units, magnets, vacuum and cryosystems, insertion devices and beam-lines; in-short, many of the sub-systems required to manufacture a proton beam therapy system. Accel has elected to provide a turn key solution for proton therapy systems. Accel's first system is located at the Rinecker Proton Therapy Center, in Munich, Germany which will be the first clinically driven proton facility in Europe. Varian/Accel proton therapy equipment does not yet have FDA clearance.

**PERFORMA FINANCIAL STATEMENTS  
FOR FIVE YEARS ENDING**

**Balance Sheet**

|                                               | Year One             | Year Two             | Year Three           | Year Four            | Year Five            |
|-----------------------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| <b>ASSETS</b>                                 |                      |                      |                      |                      |                      |
| <b><u>Current Assets</u></b>                  |                      |                      |                      |                      |                      |
| Cash                                          | \$67,739,871         | \$161,460,392        | \$324,812,369        | \$392,139,127        | \$566,673,713        |
| Accounts Receivable                           | 160,000,000          | 160,000,000          | 166,000,000          | 180,000,000          | 208,000,000          |
| <b>Total Current Assets</b>                   | <b>227,739,871</b>   | <b>321,460,392</b>   | <b>490,812,369</b>   | <b>572,139,127</b>   | <b>774,673,713</b>   |
| <b><u>Other Current Assets</u></b>            |                      |                      |                      |                      |                      |
| JV European Partners                          | 1,445,000            | 3,075,000            | 4,635,000            | 6,615,000            | 9,015,000            |
| <b>Total Other Current Assets</b>             | <b>1,445,000</b>     | <b>3,075,000</b>     | <b>4,635,000</b>     | <b>6,615,000</b>     | <b>9,015,000</b>     |
| <b><u>Property, Plant &amp; Equipment</u></b> |                      |                      |                      |                      |                      |
| Buildings                                     | 0                    | 5,000,000            | 10,000,000           | 10,000,000           | 10,000,000           |
| Furniture & Fixtures                          | 500,000              | 1,000,000            | 1,500,000            | 1,500,000            | 1,500,000            |
| Computers                                     | 500,000              | 1,000,000            | 1,500,000            | 3,000,000            | 4,500,000            |
| Software                                      | 150,000              | 300,000              | 450,000              | 750,000              | 1,050,000            |
| Licensing                                     | 5,000,000            | 10,000,000           | 15,000,000           | 20,000,000           | 25,000,000           |
| <b>Sub Total</b>                              | <b>6,150,000</b>     | <b>17,300,000</b>    | <b>28,450,000</b>    | <b>35,250,000</b>    | <b>42,050,000</b>    |
| Less: Accumulated Depreciation                | 0                    | 513,333              | 1,740,000            | 4,500,000            | 7,133,333            |
| <b>Total Property, Plant &amp; Equipment</b>  | <b>6,150,000</b>     | <b>16,786,667</b>    | <b>26,710,000</b>    | <b>30,750,000</b>    | <b>34,916,667</b>    |
| <b>Total Assets</b>                           | <b>\$235,334,871</b> | <b>\$341,322,058</b> | <b>\$522,157,369</b> | <b>\$609,504,127</b> | <b>\$818,605,380</b> |
| <b>LIABILITIES &amp; EQUITY</b>               |                      |                      |                      |                      |                      |
| <b><u>Current Liabilities</u></b>             |                      |                      |                      |                      |                      |
| Accounts Payable                              | \$3,950,000          | \$44,212,205         | \$44,952,720         | \$33,740,079         | \$85,401,445         |
| Equipment Payable                             | \$120,000,000        | \$127,000,000        | \$125,000,000        | \$150,000,000        | \$180,000,000        |
| Income Tax Payable                            | 33,962,205           | 32,440,516           | 35,187,359           | 38,061,365           | 57,925,438           |
| <b>Total Current Liabilities</b>              | <b>157,912,205</b>   | <b>203,652,721</b>   | <b>205,140,079</b>   | <b>221,801,444</b>   | <b>323,326,883</b>   |
| <b>Total Liabilities</b>                      | <b>157,912,205</b>   | <b>203,652,721</b>   | <b>205,140,079</b>   | <b>221,801,444</b>   | <b>323,326,883</b>   |
| <b>STOCKHOLDERS EQUITY</b>                    |                      |                      |                      |                      |                      |
| Common Stock                                  | 0                    | 0                    | 0                    | 0                    | 0                    |
| Paid in Capital                               | 14,350,000           | 14,350,000           | 128,350,000          | 128,350,000          | 128,350,000          |
| <b><u>Retained Earnings</u></b>               |                      |                      |                      |                      |                      |
| Beginning Retained Earnings                   | 0                    | 63,072,666           | 123,319,338          | 188,667,290          | 259,352,683          |
| Current Year Net Income (Loss)                | 63,072,666           | 60,246,672           | 65,347,952           | 70,685,393           | 107,575,814          |
| Ending Retained Earnings                      | 63,072,666           | 123,319,338          | 188,667,290          | 259,352,683          | 366,928,497          |
| <b>Total Stockholders Equity</b>              | <b>77,422,666</b>    | <b>137,669,338</b>   | <b>317,017,290</b>   | <b>387,702,683</b>   | <b>495,278,497</b>   |

|                                                   |                             |                             |                             |                             |                             |
|---------------------------------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| <b>Total Liabilities&amp; Stockholders Equity</b> | <b><u>\$235,334,871</u></b> | <b><u>\$341,322,058</u></b> | <b><u>\$522,157,369</u></b> | <b><u>\$609,504,127</u></b> | <b><u>\$818,605,380</u></b> |
|---------------------------------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|

## OPERATING STATEMENT

|                                   | <b>Year One</b>            | <b>Year Two</b>            | <b>Year Three</b>          | <b>Year Four</b>           | <b>Year Five</b>            |
|-----------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|-----------------------------|
| <b>Gross Revenues</b>             |                            |                            |                            |                            |                             |
| Forecast Multi Rooms              | \$100,000,000              | \$160,000,000              | \$160,000,000              | \$160,000,000              | \$220,000,000               |
| Forecast Single Room              | 0                          | 40,000,000                 | 60,000,000                 | 80,000,000                 | 120,000,000                 |
| Service Revenue                   | <u>0</u>                   | <u>0</u>                   | <u>0</u>                   | <u>500,000</u>             | <u>9,500,000</u>            |
| <b>Total Gross Revenues</b>       | <b>200,000,000</b>         | <b>200,000,000</b>         | <b>220,000,000</b>         | <b>240,500,000</b>         | <b>349,500,000</b>          |
| <b>Cost of Sales</b>              | 100,000,000                | 100,000,000                | 110,000,000                | 120,000,000                | 170,000,000                 |
| <b>Gross Margin</b>               | <u>100,000,000</u>         | <u>100,000,000</u>         | <u>110,000,000</u>         | <u>120,500,000</u>         | <u>179,500,000</u>          |
| <b>Operating Expenses</b>         | 2,965,129                  | 7,312,813                  | 9,464,689                  | 11,753,242                 | 13,998,747                  |
| <b>Operating Income</b>           | <u>97,034,871</u>          | <u>92,687,187</u>          | <u>100,535,311</u>         | <u>108,746,758</u>         | <u>165,501,253</u>          |
| <b>Other Income &amp; Expense</b> | 0                          | 0                          | 0                          | 0                          | 0                           |
| <b>Income Before Taxes</b>        | <u>97,034,871</u>          | <u>92,687,187</u>          | <u>100,535,311</u>         | <u>108,746,758</u>         | <u>165,501,253</u>          |
| <b>Income Taxes (35%)</b>         | <u>33,962,205</u>          | <u>32,440,516</u>          | <u>35,187,359</u>          | <u>38,061,365</u>          | <u>57,925,438</u>           |
| <b>Net Income</b>                 | <u><u>\$63,072,666</u></u> | <u><u>\$60,246,672</u></u> | <u><u>\$65,347,952</u></u> | <u><u>\$70,685,393</u></u> | <u><u>\$107,575,814</u></u> |