

Request for Expedited Grant

EnteroMedics Inc.

Introduction

EnteroMedics Inc. has requested an experimental license for the Maestro™ Obesity Management System, a medical device under development for the treatment of obesity. A surgically implanted module applies a high-frequency electrical current to the vagus nerve, which runs between the brain and digestive tract, rendering the nerve unable to propagate a signal. Early trials (conducted outside the United States) show significant weight loss.

The implanted device is powered by an external unit, carried in a holster or “fanny pack,” that transmits RF through the skin at 6.78 MHz, an ISM frequency. This operation complies with Part 18 of the Commission’s Rules. For brief intervals (duty cycle 0.004%), the same 6.78 MHz signal is AM modulated to send data to the implanted device. Communication in the other direction (duty cycle 3.1%) uses “load shift keying,” in which the implanted module presents a varying load to the external unit. During both types of communications, the radiated emissions in the 6.78 MHz band exceed the limits of Part 15. (Out-of-band emissions *do* comply with Section 15.209.)

EnteroMedics has completed preliminary studies in Mexico, Australia, and Norway. The device is now ready for FDA-regulated clinical studies in the United States.

We request an expedited grant to commence clinical trials of a treatment for a leading cause of preventable death. It is no exaggeration to say that a swift grant of the license will very probably save lives.

Obesity as a Serious Medical Issue

The following facts about obesity help to place the problem in perspective:

- Published estimates of deaths related to obesity in the United States range from 112,000 to 400,000 per year, making obesity one of the leading causes of preventable death.ⁱ
- Two-thirds of adults in the U.S. (65.7%) are either obese (BMI ≥ 30.0 kg/m²) or overweight (BMI 25.0-29.9). One in twenty people in the U.S. is categorized as extremely obese (BMI ≥ 40).ⁱⁱ
- Recent studies document the morbidity and mortality associated with BMI over 35, as well as the potential benefits accruing to the metabolism once significant weight loss is achieved.^{iii,iv}
- The prevalence of children and adolescents who are overweight has increased more than two-fold since 1976.^v
- There is a well-established association between obesity and clinically significant diseases, *e.g.*, type 2 diabetes, hypertension and, osteoarthritis – three leading causes of morbidity and mortality in industrialized countries.^{vi}

- Patients who are obese incur 37% more health care costs than people with normal weight, and spending on obese patients accounted for 27% of the growth in inflation-adjusted per capita health care spending between 1987 and 2001.^{vii}
- The public health and therapeutic challenges posed by obesity continue to be the focus of treatment guidelines.^{viii,ix}
- *The currently available treatment options do not meet the needs of many obese patients.*^x

Finding a successful obesity treatment continues to challenge both health care providers and patients. Diet and exercise programs may result in short-term weight loss but are associated with slow, inexorable regain of body weight for most people.^{xi}

Drug therapy has also resulted in only limited success and modest weight loss for the obese patient population. An analysis of published data shows that drug therapy results in between 2.8 and 3.6 kg (6 lbs to 8 lbs) of weight loss after 1 year.^{xii} Death or other serious adverse events have been reported with drug therapy. In cases such as “fen-phen” (fenfluramine-phentermine) and “PPA” (phenylpropanolamine), adverse events resulted in removal from the market.

Bariatric surgery has been performed since the 1960s. In 2003, the number of bariatric surgeries had reached 103,000, and 144,000 such procedures were projected by the end of 2004.^{xiii,xiv,xv} Gastric bypass surgery is the most common procedure in the U.S. It results in substantial and sustained weight loss, but is also associated with significant morbidity and mortality, with 30-day mortality rates reported to range from below 1.0% to 1.9% or more depending on the experience of the surgeon and the annual number of procedures performed at the hospital.^{xvi,xvii,xviii} Gastric banding, which is done more commonly outside the U.S., is also effective but results in significantly less weight loss, both short- and long-term, than the gastric bypass operation.^{xix} Patients may require frequent adjustments of their gastric bands. Furthermore, a number of patients regain weight following gastric banding because they adapt to the gastric constriction.

Clinical results on 31 subjects with 6 months of Maestro therapy

EnteroMedics has conducted an initial study outside the U.S. on 31 subjects implanted with the Maestro System and followed for a 6-month treatment period. The subjects were patients who had not responded to other weight-management measures, including dietary counseling and drug therapy. The three investigational sites were:

- Department of Surgery Instituto Nacional de la Nutrición Salvador Zubiran (INNSZ), Mexico City, Mexico,
- Adelaide Bariatric Center, Flinder’s Private Hospital, Adelaide, Australia,
- National Center for Advanced Laparoscopic Surgery, St. Olav’s University Hospital, Trondheim, Norway.

The clinical trial was conducted according to all local laws and regulations. The conduct of the study was closely monitored. An independent Safety Monitoring Board (SMB) was established prior to the initiation of the trial and met regularly to assess the ongoing safety information collected during the trial.

On average, patients had lost more than 13 lbs after 6 months of Maestro therapy. The SMB reviewed and adjudicated all serious adverse events. No deaths, no unanticipated adverse device effects, and no serious adverse events related to device therapy were reported during the study.

The efficacy results and safety profile of this initial clinical trial support the conduct of a larger clinical trial in patients with obesity who have not responded to standard medical management.

Conclusion

An FCC experimental license is prerequisite to commencing a U.S. clinical trial needed for FDA approval. An early grant of the license will contribute directly to bringing the benefits of the therapy to the U.S. population as quickly as possible.

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