

# EndoStim® Anti-reflux Therapy

## EndoStim is a revolutionary minimally invasive, low-energy, personalized esophageal stimulation device

### A smart therapy

Normalizes the function of the lower esophageal sphincter through neuromodulation; therapy can be personalized for each patient

### Gentle procedure

Preserves natural anatomy to avoid typical gastro-intestinal side effects of traditional anti-reflux surgery

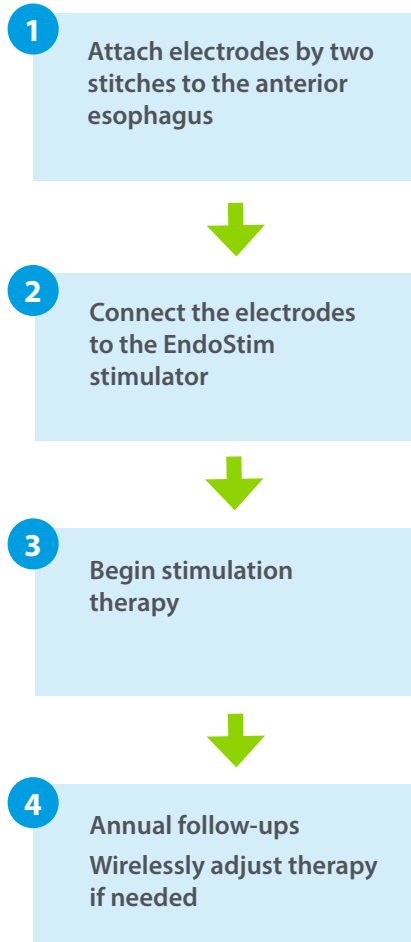
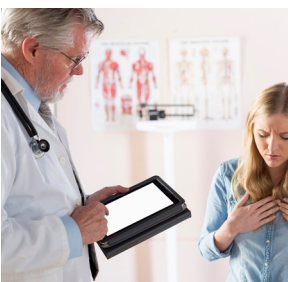
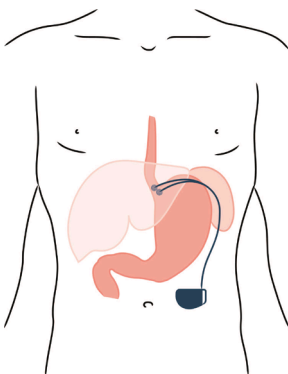
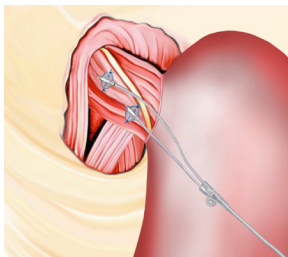
### Safe and effective

Excellent clinical outcomes in trials and in standard clinical practice. Most patients experience:

- ✓ Resolution of regurgitation and heartburn
- ✓ Significant improvement in sleep issues related to reflux
- ✓ Elimination of dependency on PPI medication
- ✓ Long-term normalization of acid exposure and sphincter function

EndoStim has been used successfully in Germany and worldwide for several years and is now enrolling patients in a registry clinical trial.

## The EndoStim Procedure



## The Lost Reflux Patient

Studies recently confirmed that approximately 30% of reflux patients are not adequately treated on PPI therapy alone.

Some of these patients suffer from debilitating symptoms despite PPI use, such as:

- sleep disruption
- ongoing regurgitation
- ongoing heartburn
- vocal impairment
- respiratory complications

Many of these patients have not yet been given the opportunity for specific reflux diagnostics nor additional therapy options aside from their PPI.

Electrical stimulation technology that has transformed cardiac rhythm and pain management is now offered as a new minimally-invasive treatment for reflux that can normalize esophageal function.

## Ideal EndoStim Candidate

- ✓ On daily PPI therapy for >1 year and dissatisfied with PPI
- ✓ NERD or esophagitis LA Grade A-C
- ✓ No hernia or hernia which can be corrected during the procedure
- ✓ GERD by pathological pH (24-hour pH <4.0 for >4.0% or DeMeester Score >14 off-PPI)

## Additional Patient Groups

- GERD in bariatric sleeve patients
- Extra-esophageal symptoms
- Esophageal dysmotility

**EndoStim®**

Stimulating reflux care ●●●●●

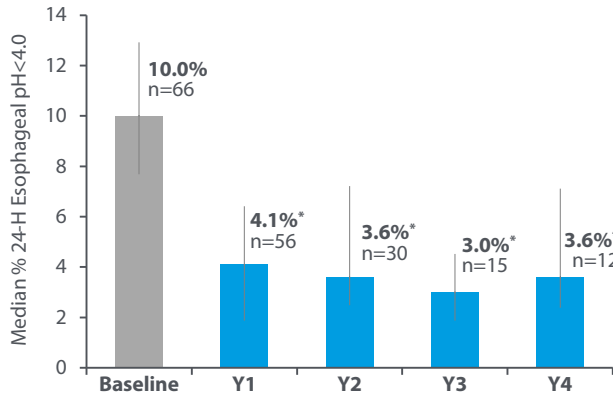
●●●●● Transforming lives

## International clinical results

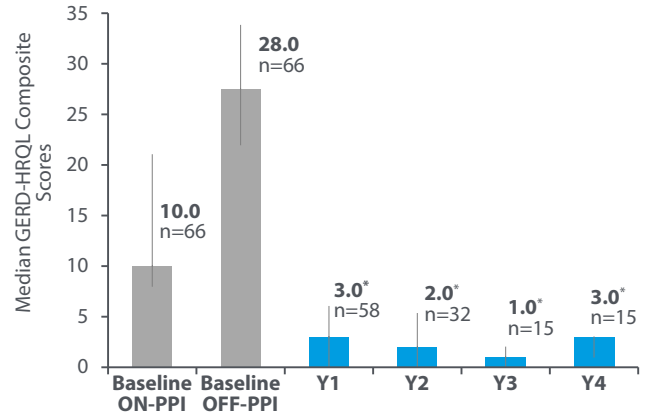
### Meta analysis of 2 published trials: Significant Improvement in GERD Symptoms and Esophageal pH

66 patients from 11 centers in 2 long-term clinical trials up to 4 years of follow-up

#### Sustained improvement in esophageal acid exposure



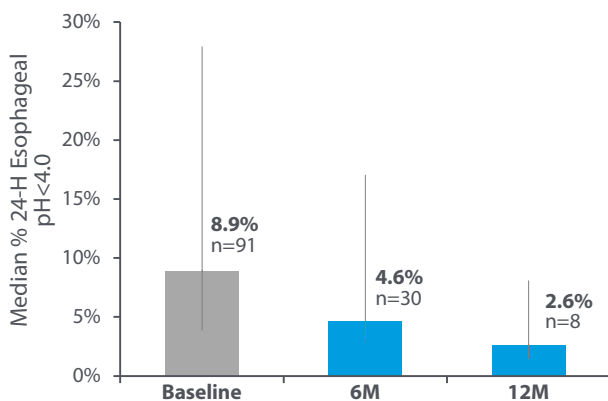
#### Sustained improvement in GERD outcomes (GERD-HRQL)



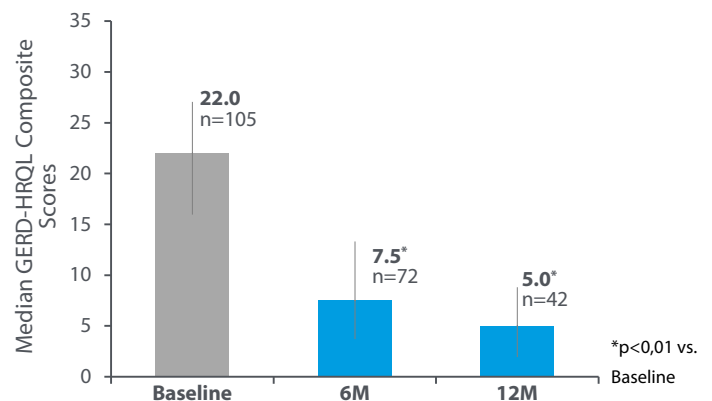
### Outcomes from ongoing multicenter commercial patient registry confirm results of the 2 long-term studies

Data from ongoing post-market patient registry including 11 sites in Germany, Denmark, Netherlands, Mexico, Argentina, confirm results of the clinical trials (accepted for presentation)

#### Sustained improvement in esophageal acid exposure



#### Sustained improvement in GERD outcomes (GERD-HRQL)



#### Select Publications, LES Stimulation Therapy

Soffer E, et al. Effect of electrical stimulation of the lower esophageal sphincter in gastroesophageal reflux disease patients refractory to proton pump inhibitors. *World J Gastrointest Pharmacol Ther.* 2016;7(1): 145-155.

Kim SE, et al. Electrical stimulation for gastroesophageal reflux disease: current state of the art. *Clin Exp Gastroenterol.* 2016; 9:11-19.

Rodríguez L, et al. Electrical stimulation therapy of the lower esophageal sphincter is successful in treating GERD: long-term 3 year results. *Surg Endosc.* 2015; DOI 10.1007/s00464-015-4539-5.

Kappelle W, et al. Electrical Stimulation Therapy of the Lower Esophageal Sphincter for refractory gastro-esophageal reflux disease – Interim Results of an International Multicenter Trial. *Aliment Pharmacol Ther.* 2015 Sep;42(5):614-25.

Rodríguez L, et al. Two-year results of intermittent electrical stimulation of the lower esophageal sphincter treatment of gastroesophageal reflux disease. *Surgery.* 2015; 157(3):556-567.

Hoppo T, et al. Long-term results of electrical stimulation of the lower esophageal sphincter for treatment of proximal GERD. *Surg Endosc.* 2014; 28(12):293-301.

Ciotola F, et al. Electrical stimulation to increase lower esophageal sphincter pressure after POEM. *Surg Endosc.* 2015; 29(1):230-235.

Rinsma NF, et al. Electrical Stimulation Therapy for Gastroesophageal Reflux Disease. *J Neurogastroenterol Motil.* 2014; 20(3):287-93.

Eypasch E. Electrical stimulation of the lower oesophageal sphincter: an emerging therapy for treatment of GORD. *Eur Surg.* 2014; 46:57-64.

Banerjee R, et al. Effect of electrical stimulation of the lower esophageal sphincter using endoscopically implanted temporary stimulation leads in patients with reflux disease. *Surg Endosc.* 2014; 28(3):1003-9.

Crowell MD. Implanted electrical devices and gastroesophageal reflux disease: an effective approach to treatment. *Expert Rev Gastroenterol Hepatol.* 2013; 7(3):189-191.

Rodríguez L, et al. Long-term results of electrical stimulation of the lower esophageal sphincter for the treatment of gastroesophageal reflux disease. *Endoscopy.* 2013; 45:595:604.

Rodríguez L, et al. Electrical stimulation therapy of the lower esophageal sphincter is successful in treating GERD: final results of open-label prospective trial. *Surg Endosc.* 2013; 27(4):1083-1092.

Rodríguez L, et al. Short-term electrical stimulation of the lower esophageal sphincter increases sphincter pressure in patients with gastroesophageal reflux disease. *Neurogastroenterol Motil.* 2012; 24(5):446-450.

Siersema PD, et al. Electrical Stimulation Therapy (EST) of the Lower Esophageal Sphincter (LES) for Refractory GERD – One Year Results of an International Multicenter Trial. *Gastroenterology.* 2016; 150(4):S216.

Rinsma NF, et al. Effect of Electrical Stimulation Therapy of the Lower Esophageal Sphincter on Postprandial Reflux Mechanisms in GERD Patients. *Gastroenterology.* 2016; 150(4):S478.

Rodríguez L, et al. Electrical Stimulation Therapy (EST) of the Lower Esophageal Sphincter (LES) is Successful in Treating GERD - Long-term 4 Year Results. *Gastroenterology.* 2016; 150(4):S476.

Labenz J, et al. Preliminary Results of a Prospective Multi-Center Observational Registry of Lower Esophageal Sphincter Stimulation for GERD: The Less-GERD Registry. *Gastroenterology.* 2016; 150(4):S478.

Nieponice A, et al. EndoStim LES Stimulation Therapy Improves GERD in Patients with Laparoscopic Sleeve Gastrectomy (LSG). *Surg Endosc.* 2016; 30:S263.

Attwood SE, et al. Global clinical experience with EndoStim lower esophageal sphincter stimulation therapy: an individual patient data meta-analysis of the open label clinical trials. *UEG Journal.* 2015; 3(5):A295.

Bouvy N, et al. Lower Esophageal Sphincter (LES) Electrical Stimulation improves sleep quality, work productivity, and quality of life in patients with refractory GERD. *UEG Journal.* 2014; 2(15):A577.

Additional data on file.