The ANIMAL study strongly underlines its effective mode of action in creating a full barrier with the surrounding tissues, preventing axonal sprouting and avoiding the formation of end-neuroma. 3, 6 and 12 months post implantation histology underlines NEUROCAP®’s action as effective barrier for unwanted nerve outgrowth.

**Objective**
- A randomized controlled study. It was aimed to assess the implantation effects of the NEUROCAP® device in a rat sciatic nerve model after 12 weeks, 6 months, and 12 months.

**Participating centers**
- VA Portland (US) - Dr. Peterson

**Endpoints**
- Procedural data, Adverse events, Clinical observations, Histopathology

**Observations and final conclusions**
- No adverse procedural observations, clinical observations, or other adverse events that were attributed to the use of NEUROCAP® throughout the duration of the study.
- Chaotic fascicle score increased in controls and decreased in the NEUROCAP® group over 12 mo.
- Inflammation score remained low in controls and decreased in NEUROCAP® group.
- Nerve outgrowth score significantly higher in control group compared to NEUROCAP® group.
- No neuromas in NEUROCAP® group at any time point (control group: 23% at 3-mo; 38% at 6-mo; 100% at 12-mo).
- NEUROCAP® treated nerve seem to become more organized with absence of neuroma formation (in contrast to the control nerve).
- Publication in preparation.

**Evidence Based Performance**

At 3 months, the device blocks sprouting by acting as physical and mechanical barrier.

At 6 months, NEUROCAP treated nerve-end stump shows organized fibers.

At 12 months, NEUROCAP treated nerve-end is organized and atrophied without neuroma formation.

NEUROCAP® is available in a diameter range of 1.5 - 8 mm.
Neuromas are a highly disabling problem. Symptomatic neuromas may develop after a nerve dissection following any trauma to a peripheral nerve, whether accidental or planned (e.g. surgery). Neuromas induced by traumatic events are incredibly distressing for patients daily life and socioeconomic functioning. The incidence of symptomatic neuromas after peripheral nerve injury is estimated to be 30%, however certain surgeries (e.g. autograft procedures, amputations) traumatize peripheral nerves and may have up to a 30% incidence rate. On average, patients experience pain severity of minimal improvement.

NEUROCAP® design is straightforward, simple and effective. NEUROCAP® is intended to protect a peripheral nerve end and to separate the nerve from surrounding environment to reduce the development of a symptomatic neuroma. NEUROCAP® is a transparent tubular device with an open end and a closed end. Dislocation of the nerve stump is prevented by suturing the nerve end into the cap. A hole at the sealed end of the tube allows for easy fixation of the nerve stump with a suture to the surrounding tissue. This allows an effective capping technique without the necessity of excessive manipulation or sacrificing other tissue. Currently, there is no gold standard for nerve treatment: lancing of the nerve stump is the most common procedure.

NEUROCAP®’s unique features support important clinical needs:
- Made of non-inflammatory flexible and biocompatible copolymers with an excellent safety record track of implementation in other medical devices
- Transparent and simple design for easy handling and optimal nerve positioning during the procedure
- Controlled mechanical strength and flexibility prevent (s) easy straining of the adhesion of the nerve into end-muscle and scar tissue
- Predictable bioresorbability to support a suitable encapsulation of the nerve stump
- Long-term groin and clinical follow-up (at least 12 months) induce an effective barrier function and considerable and lasting pain reduction in treated patients

NEUROCAP® is the only clinically proven nerve capping device. A strong body of evidence supports the effectiveness of NEUROCAP®:
- Pivotal clinical data of the STOP Neuroma Trial: this pivotal study reveals reduction of symptomatic pain over a year clinical follow up
- The PROTECT NEURO study, a multicenter post-market clinical follow-up study in both the US and Europe, is designed to strengthen and expand the clinical value of NEUROCAP® in the upper and lower extremities over a 2-year period of patient monitoring. Preliminary enrollment of this PMS study successfully concluded in summer 2018.
- The modes of action of the device, creating a full barrier with the surrounding tissues, preventing scarring and avoiding the formation of end-neuroma, is clearly demonstrated in a rat sciatic nerve model and is currently prepared for publication.

PROTECT NEURO post-market study: first preliminary results confirm the pivotal STOP Neuroma outcomes

| Endpoints | Primary endpoints (3, 6, 12, 24 mo FU) | Secondary endpoints 
|------------|-------------------------------------|-----------------------------------------------------------|
| • Final data: available during Q3-2020 | • Reduction of pain caused by symptomatic neuroma (VAS) | • Efficacy score
| • Last patient, last follow up: expected July-2020 | • Rate of recurrence of painful neuroma | • Rate of recurrence of painful neuroma
| • Patient enrollment concluded in July-2018 | • Reduction of pain caused by symptomatic neuroma (VAS) | • Patient enrollment
| • Ease of use and physician satisfaction | • Reduction of pain caused by symptomatic neuroma (VAS) | • Rate of recurrence of painful neuroma
| • Rate of recurrence of painful neuroma | • Medication use | • Efficacy of use and physician satisfaction
| • Reduction of pain caused by symptomatic neuroma (VAS) | • Medication use | • Drug Administration/Good Clinical Practice
| • Medication use | • Ease of use and physician satisfaction |• Efficacy of use and physician satisfaction

Timelines
- Patient enrollment concluded in July 2018
- Last patient, last follow up expected July-2020
- Final data: available during Q3-2020

Variable
- **Mean ± SD**
- **Variable screening** (N=73)
- **VAS**
- **QuickDash**
- **Grip strength**
- **Effect**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD (N=73)</th>
<th>Mean ± SD (N=49)</th>
<th>Mean ± SD (N=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td>17.6 ± 17.6</td>
<td>16.1 ± 21.7</td>
<td>26.7 ± 26.7</td>
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<tr>
<td>QuickDash</td>
<td>56.5 ± 20.6</td>
<td>30.2 ± 26.7</td>
<td>59.7 ± 26.7</td>
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<tr>
<td>Grip strength</td>
<td>11.9 ± 2.0</td>
<td>11.6 ± 2.0</td>
<td>9.2 ± 1.6</td>
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<tr>
<td>Effect</td>
<td>12.0 ± 3.7</td>
<td>5.2 ± 4.2</td>
<td>8.8 ± 5.1</td>
</tr>
</tbody>
</table>

* New device related SF at 6 months after external nerve cut in an animal model. Equally treated between P and 6 month follow-up.
** Uncertainty on the final shunt and instrumentation: condensation, hematoma, tension induced neuroma.
*** Secondary endpoints.
**** Primary endpoints determined at 12 months after external nerve cut in an animal model. Equally treated between P and 6 month follow-up.
***** Secondary endpoints determined at 24 months after external nerve cut in an animal model. Equally treated between P and 6 month follow-up.

**An additional 180-mm long tunnel was created at the surgical site to create a longer tunnel length (180 mm) than the alternative surgical technique (110 mm).**