Chronic Low Back Pain

Target Cause, Not Just Symptoms

ReActiv8®

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Mainstay Medical - Summary

• Chronic Low Back Pain is a huge opportunity.
  ▪ Large unmet clinical need for non-surgical CLBP
  ▪ High value target physician customers
• Our Product - ReActiv8® - restorative neurostimulation
  ▪ Solid science foundation
  ▪ Growing a strong intellectual property portfolio
  ▪ The only approved (CE Mark) implantable neurostimulation system targeting cause, not just symptoms, of Chronic Low Back Pain
• ReActiv8-A clinical trial shows clinically important, statistically significant, and lasting improvement in disability, quality of life and pain.
• Commercialization under way – first sales in Germany and Ireland
• US approval via PMA. Enrolment well under way, results expected in 2018.

CAUTION – in the United States, ReActiv8 is limited by federal law to investigational use only.
Mainstay’s ReActiv8 implantable neurostimulator is a new, unique approach to treat Chronic Low Back Pain

Please refer to the Company’s web site www.mainstay-medical.com for more information about ReActiv8
Multifidus Muscles Stabilize the Spine
Muscle Control Impairment and CLBP

- Pain from a strain or sprain injury can lead to muscle control disruption and weakening
- The multifidus muscle is the strongest stabilizer of the lumbar spine
- Atrophied multifidus is seen in 80% of CLBP patients
- Unstable spine joints can move outside their “pain-free range” resulting in more pain and re-injury leading to a continuing cycle of chronic pain:

Strong Science leads to ReActiv8

Multifidus muscle control exercises can ameliorate chronic low back pain
• Several studies show reduction in low back pain and disability\(^1\)
• Good science but challenging technique and doesn’t work for all

Electrical stimulation can reactivate muscle control
• Shown with the quadriceps (knee)\(^2\)
• Effective therapy to restore muscle control after knee surgery\(^3\)

ReActiv8 uses electrical stimulation to help reactivate the multifidus muscle control system to stabilize the spine and reduce pain

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ReActiv8 – Implantable Neurostimulator

- Minor surgical procedure, short hospital stay
- 30 minutes stimulation session, twice a day
- Remote control used to start/stop stimulation
- Not spinal cord stimulation (SCS)

Electrical stimulation delivered through leads to electrodes adjacent to nerves elicits muscle contraction.
Who are the Candidates for ReActiv8?

Typical profile:
- Relatively young
- Back pain for over a decade
- Tried most or all available treatments (e.g.: physical therapy, drugs, chiropractic, acupuncture, massage, meditation)

Physicians will look for:
- Signs of disruption in control of spine stabilizing muscles on simple office based physical movement tests
- MRI does not show pathology or structural defects
- No prior back surgery and are not candidates now
- Pain from structures in and around the back joints
- Not predominantly neuropathic pain (i.e.: not SCS candidates)
Large Underserved Potential Market

- Large number of people with disabling Chronic Low Back Pain. Prevalence ≈6% of population
- Only ≈15% of people with CLBP are suitable for spine surgery. *
- Spine surgery device market about $12.5Bn today. #
- Spinal Cord Stimulation (SCS) typically used for neuropathic pain (e.g. Failed Back Surgery). About $1.4Bn market today. #
- ReActiv8 is for people without indications for spine surgery or SCS who have continuing pain despite medical management

Company estimates ≈ 2 million candidates for ReActiv8 in US and EU today

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Back Pain Patients see many Physicians

Mainstay Customers

Consolidating into Multi-Disciplinary Spine Centers

>700 Multi-Disciplinary Spine Centers in USA, western Europe and Australia
ReActiv8-A Clinical Trial - Led to CE Marking

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic (n=53)</th>
<th>Mean ± SD or n (%)</th>
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<tbody>
<tr>
<td>Age</td>
<td>44 ± 10</td>
</tr>
<tr>
<td>Gender (Male – Female)</td>
<td>43% - 57%</td>
</tr>
<tr>
<td>Duration of Back Pain (years)</td>
<td>14 ± 11</td>
</tr>
<tr>
<td>Average Back Pain NRS</td>
<td>6.8 ± 1.2</td>
</tr>
<tr>
<td>Disability on Oswestry Disability Index (ODI)</td>
<td>44.9 ± 10.5</td>
</tr>
<tr>
<td>Quality of Life on EQ-5D</td>
<td>0.434 ± 0.185</td>
</tr>
<tr>
<td>Back Pain Medications</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>70%</td>
</tr>
<tr>
<td>Analgesics</td>
<td>59%</td>
</tr>
<tr>
<td>Non-Steroid Anti-Inflammatory Drugs (NSAIDS)</td>
<td>38%</td>
</tr>
</tbody>
</table>

A population of relatively young people who have suffered from disabling low back pain for over a decade, are not candidates for back surgery or spinal cord stimulation, most are now taking strong medications for back pain, and have attempted many other treatment options.
Disability – Clinically Important Improvement

% of subjects with a clinically important improvement in Disability (ODI)

<table>
<thead>
<tr>
<th>Time</th>
<th>% of Subjects</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 days</td>
<td>52%</td>
<td>52</td>
</tr>
<tr>
<td>6 months</td>
<td>57%</td>
<td>51</td>
</tr>
<tr>
<td>1 year</td>
<td>60%</td>
<td>47</td>
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</tbody>
</table>

Disability - Clinically Important Improvement

Quality of Life – Clinically Important Improvement

% of subjects with a clinically important improvement\(^1\) in quality of life (EQ-5D)

- **90 days** (n=52): 88%
- **6 months** (n=51): 82%
- **1 year** (n=47): 81%

Low back pain – Clinically Important Improvement

% of subjects with a clinically important improvement\(^1\) in Low Back Pain (NRS)

- **90 days** (n=52): 63%
- **6 months** (n=51): 61%
- **1 year** (n=47): 57%

**Average NRS ± SE**

- Baseline (N=53)
- 90 days (N=52)
- 6 months (N=51)
- 1 year (N=47)

\(\* \text{P} \ < \ 0.001\)

Summary Results

Patients can do more, have less pain and a better quality of life.

Proportion of subjects with clinically important improvement in one, two or three key endpoints (NRS, ODI, EQ-5D)

<table>
<thead>
<tr>
<th></th>
<th>90 Days</th>
<th>6 Months</th>
<th>1 Year</th>
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</thead>
<tbody>
<tr>
<td>40%</td>
<td>94%</td>
<td>86%</td>
<td>47%</td>
</tr>
<tr>
<td>29%</td>
<td>24%</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>25%</td>
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</table>

Doctors see patients satisfied with the therapy for a long time.

Treatment satisfaction (subject assessment)

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<tr>
<th></th>
<th>90 Days</th>
<th>6 Months</th>
<th>1 Year</th>
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<tbody>
<tr>
<td>73%</td>
<td>73%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>Very Satisfied</td>
<td>89% Satisfied</td>
<td>85%</td>
<td>81%</td>
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Europe Commercialisation

Two phases:
- Build champions in key multidisciplinary spine centers
- Expansion based on ReActiv8 champions and powerful data

First target market is Germany
- Direct sales force in place, augmented by field clinical support staff
- Using existing reimbursement codes
- Build evidence with registry and other clinical trials

Expanding to other markets
- Use existing reimbursement codes where available
- Seek new codes when higher level of evidence is available
US Commercialisation

US Approval via PMA path

ReActiv8-B Clinical Trial (description next page)

- 128 Pivotal Subjects for PMA submission
- Interim look when outcome data from 50% of subjects
- If successful, will produce Level 1 Clinical Evidence

Enrollment well under way

- 27 sites selected in US, Australia, UK, Belgium and Netherlands
- Anticipate enrollment complete around end 2017
- Anticipate results in 2018

Plan to use direct sales force in US and start with existing codes
ReActiv8-B Clinical Trial Description*

- International, multi-center, prospective, randomized, sham controlled, triple blinded trial, with one way crossover
- Primary outcome: responder analysis
  - “Responder” - a subject with ≥30% improvement in low back pain VAS without increase in drugs prescribed and taken for pain in the 14 days prior to endpoint
  - Trial is successful if difference in responder rate between treatment and control
- Control arm subjects crossed over to full stimulation at 120 days
- Multiple secondary outcomes

* See [https://clinicaltrials.gov/show/NCT02577354](https://clinicaltrials.gov/show/NCT02577354)
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