Positive Results for Mainstay Medical's Clinical Trial of ReActiv8®

Clinically important, statistically significant, and lasting improvement in pain, disability, and quality of life for people with Chronic Low Back Pain and limited treatment options

63% of people with clinically important improvement in back pain; and 72% with clinically important improvement in back pain in the cohort with no financial compensation related to back pain

Dublin – Ireland, 31 August 2015 – Mainstay Medical International plc (**Mainstay** or the **Company,** listed on Euronext Paris: MSTY.PA and ESM of the Irish Stock Exchange: MSTY.IE), a medical device company focused on bringing to market ReActiv8®, a new implantable neurostimulation system to treat disabling Chronic Low Back Pain (CLBP), today announced results from the ReActiv8-A Clinical Trial, an international, multi-centre, prospective, single arm trial to gather data for a submission for CE Marking for ReActiv8. The ReActiv8-A Trial shows clinically important, statistically significant and lasting improvement in pain, disability and quality of life in this clinically challenging population.

ReActiv8 is for treatment of people who suffer from CLBP, have attempted most or all available treatment options, and are not candidates for back surgery or spinal cord stimulation. The ReActiv8-A Trial population was relatively young (mean age 43.9 years) and had a long history of low back pain (mean 13.8 years). All of the subjects had attempted physical therapy, and 70% were taking opioids for back pain. The results presented are based on data from the first 47 subjects implanted in the ReActiv8-A Trial of whom 46 have reached the 90 day follow up and to date 33 have reached the 180 day follow up.

Results highlights:

- Clinical performance of ReActiv8 at 90 days compared to baseline for all subjects is:
  - **63%** with clinically important improvement in back pain defined as ≥2 point reduction on the 0-10 Numerical Rating Scale (NRS) for low back pain[1] measured on the day.
  - **54%** responder rate for pain: A responder is defined as a subject with a clinically important improvement in mean of prior 7 days NRS with no clinically significant increase in medications taken for low back pain.
  - **57**% with a clinically important improvement[1] in disability on the Oswestry Disability Index (ODI).
  - **67%** with a clinically important improvement[2] in quality of life on the EQ-5D scale.

- Clinical performance at 90 days is even better for the group of subjects who do not receive financial compensation for being out of work due to their back pain. For those 32 subjects the results are:
  - **72%** with clinically important improvement in low back pain NRS on the day.
  - **66%** responder rate for pain.
  - **63%** with clinically important improvement in ODI.
  - **69%** with a clinically important improvement in EQ-5D (**90%** at 180 days).

- Improvements in low back pain, disability and quality of life were generally consistent or improved at 180 days (n=33). Paired data for all subjects at 90 and 180 days respectively are:
  - **63%** and **58%** with clinically important improvement in low back pain NRS on the day.
  - **57%** and **58%** with clinically important improvement in ODI.
  - **67%** and **79%** with clinically important improvement in EQ-5D
  - **61%** and **64%** reported >50% Percent Pain Relief.

1 Dworkin, R. H., Turk, D. C., Wyrwich, K. W., Beaton, D., Cleeland, C. S., Farrar, J. T., Zavisic, S. (2008). Interpreting the clinical importance of treatment outcomes in chronic pain clinical Trials: IMMPACT recommendations. The Journal of Pain: Official Journal of the American Pain Society, 9(2), 105–21.

2 Soer, R., Reneman, M. F., Speijer, B. L. G. N., Coppes, M. H., & Vroomen, P. C. A. J. (2012). Clinimetric properties of the EuroQol-5D in patients with Chronic Low Back Pain. Spine Journal, 12(11), 1035–1039. http://doi.org/10.1016/j.spinee.2012.10.030

- Adverse Events (AEs) incidence and type were comparable to AEs in clinical trials reported for other neurostimulation devices, with no unanticipated AEs and no serious AEs related to the device, therapy or procedure.

- The observed lead migration incidence (<1%) demonstrates that the ReActiv8 lead mitigates the risk of lead migration identified with commercially available neurostimulation leads in the earlier Feasibility Trial.

- The incidence of surgical revision (19%) to date is within the range published for other neurostimulation systems. Mainstay has identified a modification to the implant technique which it believes has the potential to reduce revision rates.

A full description of the ReActiv8-A Trial and results is provided below.

The Chairman of the ReActiv8-A Data Monitoring Committee is Professor Chris Gilligan, Chief of the Division of Pain Medicine and Co-Director of the Spine Center at the Beth Israel Deaconess Medical Center of the Harvard Medical School. Commenting on the positive results he said: *"As physicians we struggle to provide solutions for people with chronic low back pain. The results from this clinical trial open the prospect of a new treatment option for clinicians and significant benefit for people suffering from chronic low back pain."*

Mainstay estimates that there are over two million people in the US and EU who could be candidates for treatment with ReActiv8. They are people with CLBP, in whom the root cause of the persistence of pain is disruption in control of the key muscles that stabilize the lumbar spine, particularly the lumbar multifidus. ReActiv8 is designed to deliver episodic electrical stimulation to nerves that cause these muscles to contract, helping to restore stability, and thus allowing recovery from CLBP.

ReActiv8 is not spinal cord stimulation. SCS targets different clinical conditions and delivers electrical stimulation to interfere with the perception of pain, without addressing the root cause. The market for SCS is estimated to be approximately $1.4Bn in 2015[3] or approximately 100,000 patients.

Dr. Marc Russo, Director of the Hunter Pain Clinic in Newcastle, Australia and investigator in the Trial said: *"It was pleasing to see ReActiv8 have such an impact on people's quality of life after so many other conventional treatments have been unsuccessful for such a long time."*

Peter Crosby, CEO of Mainstay, added: *"The results from the ReActiv8-A Trial show improvements which are better than any other therapy for this group of people as reported in the literature. We are excited that our unique approach to treating this type of chronic low back pain offers the potential to change the lives of millions of people worldwide who have no effective treatment alternative."*

The Company believes that data from the subjects reported may be sufficient to apply for a CE Mark for ReActiv8, and is engaging with its notified body about the Company's submission for CE Marking.

Subjects continue to be enrolled in the ReActiv8-A Trial to gather additional data on performance and safety which the Company plans to incorporate into the Post Market Clinical Follow Up.

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3 https://www.novationco.com/media/industryinfo/OrthoWatch_Spring2015_Spine_Neuromodulation.pdf

The Company will host a live conference call and webcast (in English) for analysts and investors on Monday, 31 August, 2015 at 2:30pm Dublin-London time (3:30pm Paris; 09:30am New York).

Dial in details for this call are:

Ireland Toll Free Number:	1800 936 842
France Toll Free Number:	0805 101 988
Finland Toll Free Number:	0800 523 133
Netherlands Toll Free Number:	0800 265 8619
USA Toll Free Number:	1866 928 7517
International Non Toll Free Number:	+44 203 139 4830
Passcode:	**70678930#**

The live webcast will be available on the "Investors" section of Mainstay Medical website at: http://www.mainstay-medical.com/investors

PR and IR Enquiries:

Consilium Strategic Communications (international strategic communications – business and trade media)

Chris Gardner, Mary-Jane Elliott, Matthew Neal, Hendrik Thys,

Tel: +44 203 709 5700 / +44 7921 697 654

Email: mainstaymedical@consilium-comms.com

FTI Consulting (for Ireland)

Jonathan Neilan,
Tel: +353 1 663 3686

Email: jonathan.neilan@fticonsulting.com

FTI Consulting (for France)

Astrid Villette,

Tel: +33 1 47 03 69 51

Email: Astrid.Villette@fticonsulting.com

Investor relations:

The Trout Group LLC

Jillian Connell,
Tel: +1 646 378 2956 / +1 617 309 8349

Email: jconnell@troutgroup.com

ESM Advisers:

Fergal Meegan or Barry Murphy, Davy

Tel: +353 1 679 6363

Email: fergal.meegan@davy.ie or barry.murphy2@davy.ie

ReActiv8-A Trial Description and Results

Subjects were enrolled in the ReActiv8-A Trial if they continued to experience disabling CLBP despite at least 90 days of medical management, which included at least physical therapy and drugs (most subjects had attempted many other treatments including chiropractic, massage, and acupuncture). In addition, subjects had no identifiable spine pathology that could be the clear cause of their CLBP, had no prior spine surgery, and were not candidates for spine surgery or spinal cord stimulation. Back pain was assessed using a Numerical Rating Scale (NRS) in which subjects were asked to grade their low back pain from 0 (no pain) to 10 (worst imaginable pain). Subjects were instructed to not change their medications for low back pain until after the 90 day end point.

Subjects were implanted with ReActiv8 in a short surgical procedure. After approximately 14 days, subjects began stimulation sessions with ReActiv8 for 30 minutes each morning and evening, and outcome data collection is at 90 days, 180 days and annually thereafter.

Baseline Characteristics

The key baseline characteristics for all 47 implanted subjects are shown in the table below.

Characteristic	**Mean ± SD or n (%)**
Age	43.9 ± 10.7
Gender (Male - Female)	21 (45%) - 26 (55%)
Duration of Back Pain (years)	13.8 ± 10.3
Average Back Pain NRS	6.9 ± 0.8
Disability on Oswestry Disability Index (ODI)	44.5 ± 10.5
Quality of Life on EQ-5D	0.47 ± 0.2
Back Pain Medications	
Opioids	33 (70%)
Analgesics	28 (60%)
Non-Steroid Anti-Inflammatory Drugs (NSAIDS)	18 (38%)

In summary, this is a population of relatively young men and women who have suffered from disabling low back pain for over a decade, have tried many other treatment options, and most now depend on strong medications for pain.

Outcomes Data

There were 47 subjects implanted, and 46 reached the 90 day end-point (one subject was explanted). Data continue to be collected, and are presented for all subjects who have reached the 90 and 180 day follow up to date. The table below highlights summary outcome data. Note that for responder rates, the proportions are presented as X/Y where X is the number of responders and Y is the number of subjects who have been assessed at that endpoint.

Outcomes – N=47 – All Subjects	*Day 90 (n=46)*	*Day 180 (n=33)*
Low back pain – prior 7 day average Numerical Rating Scale (0 – 10)		
Improvement from baseline – absolute	2.5 ± 0.3 p<0.0001	Not recorded beyond 90 days per protocol
Improvement from baseline – %	36%	
Responder Rate (% of subjects)	54% (25/46)	
Low back pain – on the day Numerical Rating Scale (0 – 10)		
Improvement from baseline - absolute	2.3 ± 0.3 p<0.0001	2.2 ± 0.5 p<0.0001
Improvement from baseline – %	33%	31%
% of subjects with ≥2 point improvement	63% (29/46)	58% (18/33)
Low back pain improvement – Percent Pain Relief (0 – 100%)		
Reported change (%)	47% ± 4.3	50% ± 5.2
% of subjects with ≥50% pain relief	61% (28/46)	64% (21/33)
Disability (Oswestry Disability Index) (0 – 100)		
Improvement from baseline	14.8 ± 2.3 p<0.0001	12.4 ± 2.8 p=0.0001
% of subjects with clinically important change	57% (26/46)	58% (19/33)
Quality of life (EQ-5D) (1 = Maximum Value)		
Improvement from baseline	0.16 ± 0.03 p<0.0001	0.15 ± 0.04 p=0.0007
% of subjects with clinically important change	67% (31/46)	79% (26/33)

Outcomes – Pain

For the 90 day endpoint, the assessment was the mean of the prior seven days of daily average low back pain NRS recorded in a Journal. For all assessments (including after 90 days), subjects were asked to report their low back pain NRS on the day. A "responder" is defined in accordance with the IMMPACT recommendations[4] as a subject with a reduction in NRS of 2 points or more from baseline, with the addition of no clinically significant increase in medications taken for low back pain.

The responder rate at 90 days was 54%, and at 180 days 58% of subjects reported ≥2 point improvement on the single day NRS.

Subjects were also asked to rate their "Percent Pain Relief" compared to baseline. By this measure, 61% of subjects reported 50% or better improvement at 90 days, and 64% reported 50% or better improvement by 180 days.

Outcome – Disability (ODI)

The Oswestry Disability Index (ODI) is a disease specific assessment of the disabling effects of back pain. The IMMPACT recommendations are that a reduction from baseline of 10 points or more constitutes an "important change".[5]

57% (26/46) of subjects had an important change in ODI at 90 days, and the mean improvement was 14.8 points. For those subjects who have reached 180 days 58% (19/33) had an important change in ODI, and the mean improvement was 12.4 points.

Outcome – Quality of Life (EQ-5D)

The European Quality of Life Assessment (EQ-5D) is commonly used as an outcome measure in studies on back pain.

67% (31/46) of subjects had a clinically important improvement in EQ-5D at 90 days, and the mean improvement was 0.16 ± 0.03. For those subjects who have reached 180 days, 79% (26/33) had a clinically important improvement in EQ-5D, with a mean improvement of 0.15 ± 0.04.

4 Dworkin, R. H., Turk, D. C., Wyrwich, K. W., Beaton, D., Cleeland, C. S., Farrar, J. T., Zavisic, S. (2008). Interpreting the clinical importance of treatment outcomes in chronic pain clinical Trials: IMMPACT recommendations. The Journal of Pain: Official Journal of the American Pain Society, 9(2), 105–21.

5 Ostelo, R. W. J. G., Deyo, R. A., Stratford, P., Waddell, G., Croft, P., Von Korff, M., … de Vet, H. C. W. (2008). Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine, 33(1), 90–4

Other Outcomes

The Treatment Satisfaction Questionnaire is an assessment of the subject's satisfaction with the treatment. At 90 days (n=46) 89% of subjects were satisfied, of whom 85% were very satisfied and at 180 days (n=33) 85.0% were satisfied of whom 89% were very satisfied.

The Clinical Global Impression is the physician's assessment of the subject compared to baseline, and at 90 days (n=45), 84% were rated as "better."

Effect of Financial Compensation

Analysis of the data showed significantly better outcomes in subjects who were not receiving financial compensation for being out of work due to their back pain. There is consistent evidence in scientific literature that financial compensation for a change in work status due to back pain is a strong predictor for treatment failure in clinical trials of pain therapies. Therefore it has become usual practice in clinical trials of therapies for pain (including recent spinal cord stimulation trials) to exclude subjects with financial compensation.[6,7]

In the ReActiv8-A Trial, there were 15 subjects who were receiving financial compensation for being out of work due to their back pain. The 90 day mean improvement in NRS for this group (the "Financial Compensation Cohort)" was 1.4 points (21% improvement), and the responder rate was 29% (4/14). In contrast, the outcomes for those not receiving financial compensation (the "Usual Cohort") were superior (p=0.05 for the 90 day NRS outcome). The 90 day mean improvement in NRS for the Usual Cohort was 3.0 points (43% improvement, and the responder rate was 66% (21/32). Summary results for the Usual Cohort are presented in the table below.

Outcomes – N=32 – Usual Cohort	Day 90 (n=32)	Day 180 (n=21)
Low back pain – prior 7 day average Numerical Rating Scale (0 – 10)		
Improvement from baseline – absolute	3.0 ± 0.4 p<0.0001	Not recorded beyond 90 days per protocol
Improvement from baseline – %	43%	
Responder Rate (% of subjects)	66% (21/32)	
Low back pain – on the day Numerical Rating Scale (0 – 10)		
Improvement from baseline - absolute	2.8 ± 0.4 p<0.0001	2.9 ± 0.6 p=0.0001
Improvement from baseline – %	40%	42%
% of subjects with ≥2 point improvement	72% (23/32)	62% (13/21)
Low back pain improvement – Percent Pain Relief (0 – 100%)		
Reported change (%)	50% ± 5.4	55% ± 6.7
% of subjects with ≥50% pain relief	63% (20/32)	71% (15/21)
Disability (Oswestry Disability Index) (0 – 100)		
Improvement from baseline	16.5 ± 2.6 p<0.0001	13.0 ± 3.7 p=0.002
% of subjects with clinically important change	63% (20/32)	57% (12/21)
Quality of life (EQ-5D) (1 = Maximum Value)		
Improvement from baseline	0.19 ± 0.03 p<0.0001	0.17 ± 0.06 p=0.0061
% of subjects with clinically important change	69% (22/32)	90% (19/21)

Subjects were also asked to rate their "Percent Pain Relief" compared to baseline. In the Usual Cohort 63% reported 50% or better improvement at 90 days, and 71% reported a 50% or better improvement by 180 days.

Adverse Events

Adverse events are adjudicated by an independent Clinical Events Committee. As of the most recent adjudication in July, there were 53 reported AEs related to the device, therapy or procedure. There were two

6 See, for example, https://clinicalTrials.gov/show/NCT01609972 and https://clinicalTrials.gov/show/NCT01923285

7 Dworkin, R. H., Turk, D. C., Peirce-Sandner, S., Baron, R., Bellamy, N., Burke, L. B., … Witter, J. (2010). Research design considerations for confirmatory chronic pain clinical Trials: IMMPACT recommendations. Pain, 149(2), 177–93.

Serious Adverse Events (SAEs), neither of which was related to the device, therapy or procedure. There were no unanticipated AEs or unanticipated device related AEs. The AE incidence and type were comparable to AEs in clinical trials reported for other neurostimulation devices.

Lead Related Events

The ReActiv8 lead has shown only one instance of lead migration (dislodgement) out of 105 implanted leads (including those implanted in revision procedures) for a lead migration incidence of less than 1%. These results demonstrate that the ReActiv8 lead mitigates the risk of lead migration identified with commercially available neurostimulation leads in the earlier Feasibility Trial.

As part of continuous testing, the ReActiv8 Implantable Pulse Generator (IPG) can detect anomalies in a lead which, in some cases, can result in loss of stimulation. Lead anomalies led to elective revision surgery in 9 subjects for a surgical revision incidence of 19%, which is comparable to published data for neurostimulation systems.[8]

In the 12 leads returned for analysis after elective revision surgery, a break in one or more wires inside the lead was found. These breaks were found not to result from the design or manufacture of the leads. In additional laboratory studies, in some cases a tight bend in the lead was observed as the lead traverses two layers of tissue that move in different directions relative to each other. A modification to the implant technique with different lead routing was developed in conjunction with investigators to mitigate the risk of this lead bending, and this modification will be used for future implants.

Summary

These results demonstrate that for a population of people with long term Chronic Low Back Pain and limited treatment options, treatment with ReActiv8 delivers clinically important, statistically significant, and lasting improvement in pain, disability, and quality of life.

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About Mainstay

Mainstay is a medical device company which is developing an innovative implantable neurostimulation system, ReActiv8®, for people with disabling Chronic Low Back Pain (CLBP). The Company is headquartered in Dublin, Ireland. It has subsidiaries operating in Ireland, the United States and Australia, and is listed on Euronext Paris (MSTY.PA) and the ESM of the Irish Stock Exchange (MSTY.IE).

About the ReActiv8-A Trial

The ReActiv8-A clinical trial is a prospective single arm clinical trial with up to 96 subjects at sites in Australia and Europe. Outcome measures for the ReActiv8-A clinical trial are assessed at a three month endpoint after activation of stimulation and compared to baseline prior to implant. Further details can be obtained at https://clinicaltrials.gov/show/NCT01985230.

About Chronic Low Back Pain

One of the recognised root causes of CLBP is impaired control by the nervous system of the muscles that dynamically stabilise the spine in the lower back, and an unstable spine can lead to back pain. ReActiv8 is designed to electrically stimulate the nerves responsible for contracting these muscles and thereby help to restore muscle control and improve dynamic spine stability, allowing the body to recover from CLBP.

People with CLBP usually have a greatly reduced quality of life and score significantly higher on scales for pain, disability, depression, anxiety and sleep disorders. Their pain and disability can persist despite the best available medical treatments, and only a small percentage of cases result from an identified pathological condition or anatomical defect that may be correctable with spine surgery. Their ability to work or be productive is seriously affected by the condition and the resulting days lost from work, disability benefits and health resource utilisation put a significant burden on individuals, families, communities, industry, and governments.

Further information can be found at www.mainstay-medical.com

8 Rosenow, J. M., & Stanton-Hicks, M, Rezai, Ali R, Henderson, J. (2006). Failure modes of spinal cord stimulation hardware. Journal of Neurosurgery. Spine, 5(3), 183–90. doi:10.3171/spi.2006.5.3.183

ReActiv8 is an investigational device and is not approved for commercialisation anywhere in the world.

CAUTION – in the United States, ReActiv8 is limited by federal law to investigational use only.

Forward looking statements

This announcement includes statements that are, or may be deemed to be, forward looking statements. These forward looking statements can be identified by the use of forward looking terminology, including the terms “anticipates”, “believes”, “estimates”, “expects”, “intends”, “may”, “plans”, “projects”, “should” or “will”, or, in each case, their negative or other variations or comparable terminology, or by discussions of strategy, plans, objectives, goals, future events or intentions. These forward looking statements include all matters that are not historical facts. They appear throughout this announcement and include, but are not limited to, statements regarding the Company’s intentions, beliefs or current expectations concerning, among other things, the Company’s results of operations, financial position, prospects, financing strategies, expectations for product design and development, regulatory applications and approvals, reimbursement arrangements, costs of sales and market penetration.

By their nature, forward looking statements involve risk and uncertainty because they relate to future events and circumstances. Forward looking statements are not guarantees of future performance and the actual results of the Company’s operations, and the development of the markets and the industry in which the Company operates, may differ materially from those described in, or suggested by, the forward looking statements contained in this announcement. In addition, even if the Company’s results of operations, financial position and growth, and the development of the markets and the industry in which the Company operates, are consistent with the forward looking statements contained in this announcement, those results or developments may not be indicative of results or developments in subsequent periods. A number of factors could cause results and developments of the Company to differ materially from those expressed or implied by the forward looking statements including, without limitation, general economic and business conditions, the global medical device market conditions, industry trends, competition, changes in law or regulation, changes in taxation regimes, the availability and cost of capital, the time required to commence and complete clinical trials, currency fluctuations, changes in its business strategy, political and economic uncertainty. The forward-looking statements herein speak only at the date of this announcement.