Agenda and Speakers

• Opening Remarks
  – *Earl R. Fender, President & CEO, VertiFlex®, Inc.*

• Moderate Spinal Stenosis
  – *Pierce D. Nunley, MD, Spine Institute of Louisiana*

• Superion® Interspinous Spacer
  – *Stephen Reitzler, VP Clinical and Regulatory Affairs, VertiFlex®, Inc.*

• Superion® ISS Study Results
  – *Glenn Stiegman, MS, VP Clinical and Regulatory Affairs, MCRA*

• Radiographic Observations in the Superion® IDE
  – *Scott Blumenthal, MD, Texas Back Institute*

• Risk / Benefit Profile
  – *Pierce D. Nunley, MD, Spine Institute of Louisiana*

• Closing Remarks
  – *Earl R. Fender, President & CEO, VertiFlex®, Inc.*
Additional Representatives

• **Medical**
  – *Nick Shamie, MD, Professor & Chief, UCLA Orthopaedic Spine Surgery*

• **Study Conduct**
  – *Leslie Zaccari, Director, Clinical Research, VertiFlex®, Inc.*
  – *Teena Augustino, President, Augos Consulting, LLC*

• **Clinical & Regulatory**
  – *Justin Eggleton, Director, Spine Regulatory Affairs, MCRA*
  – *Kevin McGowan, PhD, Director, Regulatory Affairs, MCRA*

• **Statistics**
  – *Greg Maislin, MS, MA, Principal Biostatistician, BSC*

• **Biomechanics**
  – *Lisa Ferrara, PhD, Orthokinetic Technologies, LLC*

• **Independent Core Lab**
  – *John Hipp, PhD, Chief Scientific Officer, Medical Metrics, Inc.*
The Problem

Lumbar spinal stenosis patients are suffering

Narrowing of spinal canal causes pain, weakness, immobility

1.2M annual US diagnoses

From 2000-2009 the surgical hospitalization rate for LSS increased by 30%

> 175K annual decompression surgeries

# 1 reason for spine surgery in elderly

References:
1. American Association of Neurological Surgeons.
3. American Medical Association’s RBRVS Data Manager Program 2013.
Objectives of Advisory Panel Meeting

- Substantiate trial design
- Address radiographic observations
- Prove safety, effectiveness & positive benefit / risk
Moderate Spinal Stenosis

Pierce D. Nunley, MD
Study Investigator, Superion® Trial
Associate Professor, LSUHSC
Director, Spine Institute of Louisiana
Lumbar Spinal Stenosis

• Narrowing of the spinal canal, lateral recesses, and/or neural foramina caused by degenerative disease
• Compresses spinal cord and/or spinal nerves, resulting in neurological deficit
• Symptoms include pain, numbness, paraesthesia, and loss of motor control

Stenosis Ranges from Mild, to Moderate, to Severe in Degree and Symptoms
Clinical Diagnosis of Moderate Stenosis

• Clinical Signs
  – Persistent leg, buttock, groin pain
  – May or may not have back pain
  – Symptoms are worse in extension, e.g., when walking
  – Pain is relieved in flexion

• Confirmed Radiographically
  – Reduction in spinal canal area
  – Hypertrophic facets with canal encroachment
  – Nerve root compression
Spectrum of Treatment for Spinal Stenosis

Symptom Severity Drives the Treatment Methodology
Direct Decompression Benefit/Risk Profile

Potential Benefits

• Directly decompresses the neural elements
• Effective in severe stenosis
• Proven history of reasonable effectiveness

Potential Risks

• More extensive procedure
• Increased risk in older population & patients with comorbidities
• Severe adverse event risks
  – Epidural fibrosis
  – Dural tear
  – Deep wound infection
  – Destabilize the spinal segment
  – Nerve injury
Indirect Decompression

- X-STOP® - only approved PMA device (P040001)
  - Device limits ("blocks") extension to prevent compression of neural elements
  - Relies upon no removal of ligamentum flavum or bone
  - Mitigates the risk of nerve injury, dural tears and post-operative epidural fibrosis
  - Level I clinical evidence demonstrates safety and efficacy versus non-operative control
  - Does not limit future surgical options
Difficulties in Comparing Treatment Options

• Trade off between indirect and direct decompression
  – Similar effectiveness profile
  – Risk profile poorly documented in literature
    • Suggests higher reoperation rate for indirect decompression
    • Suggests higher complication/intervention rate for direct decompression
    • Lack of Level I evidence of decompression outcomes

• Direct decompression used to treat wider range
  – Moderate / severe population

• Selection of treatment guided by other patient factors
  – Age
  – Comorbidities or other risk factors
  – Patient health and activity level
  – Spinal instability or deformity
Moderate Stenosis Disease and Treatment

- Symptom severity and specific pathology dictates the treatment
  - Decision moderated by individual patient clinical presentation and risk factors

- MORE SEVERE CASES - Direct decompression provides symptom relief via surgical removal of tissues impinging upon spinal nerves

- LESS SEVERE CASES - Indirect decompression provides symptom relief via extension-blocking

Patient Treatment Driven By Clinical Symptoms
Superion® Interspinous Spacer

Stephen Reitzler
Vice President, Clinical & Regulatory Affairs
VertiFlex®, Inc.
The Superion® Interspinous Spacer

- One-piece implant
- Available in 5 sizes, 8mm to 16mm
- Composed of Ti 6Al-4V alloy conforming to ASTM F136*
- Extensive preclinical testing

The Superion® Interspinous Spacer

• Deployment Sequence

Undeployed (Closed) Implant

Cam Lobes Rotating from Implant Body

Deployed (Open) Implant
Superion® Spacer *in situ*

Position of Superion® Spacer after implantation

Biomechanical Kinematic Analysis Demonstrated Extension Blocking
Superion® Surgical Approach
Superion® Indications

The Superion® InterSpinous Spacer (the Superion® ISS) is intended to treat skeletally mature patients suffering from pain, numbness, and / or cramping in the legs (neurogenic intermittent claudication) secondary to a diagnosis of moderate lumbar spinal stenosis, with or without Grade 1 spondylololisthesis, confirmed by X-ray, MRI and / or CT evidence of thickened ligamentum flavum, narrowed lateral recess, and / or central canal or foraminal narrowing. The Superion® ISS is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg / buttock / groin pain, numbness, and / or cramping, with or without back pain. The Superion® ISS may be implanted at one or two adjacent lumbar levels in patients in whom treatment is indicated at no more than two levels, from L1 to L5.
Selection of Control Device

- Collaborated with FDA on choice of control
- Identical indications to X-STOP® device
- Similar mechanism of action (i.e., extension blocker)
- Similar risk profile
  - Expected similar peri-operative measurements
  - Expected similar failure modes
- Predicted similar safety and effectiveness profile
  - Ability to easily compare pain and function measurements
  - Ability to easily compare safety events

Expect X-STOP® Control to Perform as Well as in the Approved IDE Study
Study Design

- Prospective, Randomized, Multi-Center
- Control: PMA-approved X-STOP® IPD®
- 1:1 Randomization
- Bayesian Non-Inferiority Statistical Design
- Training Patients (n=28)
- 190 Superion®, 201 X-STOP® patients at 31 sites
- Follow-Up at discharge, 6 weeks, 3, 6, 12, 18 and 24 mos., and annually thereafter
- Subgroup analyses: Demographics, Operative Details, Radiographic Observations
Primary Inclusion Criteria

• Moderate LSS as defined in the Inclusion Criteria
  – Failed ≥ 6 months conservative care
  – Evidence of neurogenic claudication
    • Able to sit for 50 minutes without pain
    • Able to walk 50 feet or more
    • Must experience relief in flexion
  – ZCQ Physical Function (PF) score of ≥ 2.0
  – 25% to 50% reduction in canal area compared to the adjacent levels

• Additional Inclusion Criterion
  – ≥ 45 years of age
Primary Exclusion Criteria

- Fixed motor deficit
- Stenosis which requires additional surgical intervention
- Unremitting pain in any spinal position
- Significant peripheral neuropathy or acute denervation
- Significant instability of the lumbar spine
- Pathologic fractures of the vertebrae and/or hips
- Spondylolisthesis greater than Grade 1
- Degenerative scoliosis (Cobb angle > 10° at index level)
- Osteopenia, osteoporosis
Primary Endpoint

Subject is a success if they meet all of the following conditions at **24 months**

- Clinically significant improvement in outcomes compared to baseline, as determined by meeting the criteria for ≥ 2 domains of ZCQ
  - ≥ 0.5 point improvement in physical function
  - ≥ 0.5 point improvement in symptom severity
  - Score of ≤ 2.5 points on patient satisfaction domain
- No re-ops, removals, revisions, or supplemental fixation at the index level(s)
- No clinically significant confounding treatments:
  - No epidural injections, nerve block procedures at index level, spinal cord stimulators or rhizotomies
- No major implant or procedure related complications
  - No dislodgement, migration, or deformation
  - New or persistent worsened neurological deficit at the index level
  - Spinous process fractures
  - Deep infection, death, or other permanent device attributed disability
Secondary Endpoints

• Oswestry Disability Index (ODI)
• Visual Analog Scale (VAS)
  – Back Pain
  – Leg Pain (Right and Left)
• SF - 12 Short Form Health Survey, Version 2
• VertiFlex® Patient Satisfaction Survey
Radiographic Assessments

Radiographic analysis performed by independent core laboratory, Medical Metrics, Inc. (MMI)

<table>
<thead>
<tr>
<th>Quantitative</th>
<th>Qualitative</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Angular Motion</td>
<td>- Device Condition</td>
</tr>
<tr>
<td>- Translational Motion</td>
<td>- Device Migration</td>
</tr>
<tr>
<td>- Foraminal Height</td>
<td>- Device Dislodgement</td>
</tr>
<tr>
<td>- Disc Height / Angle</td>
<td>- Spinous Process Fracture</td>
</tr>
<tr>
<td>- Spondylolisthesis</td>
<td>- Device Position</td>
</tr>
<tr>
<td>- Spinous Process Distance</td>
<td>- Cam Lobe Locking / Capture Status</td>
</tr>
<tr>
<td></td>
<td>- Bone-Implant Interface Changes</td>
</tr>
<tr>
<td></td>
<td>- Exuberant Bone Formation</td>
</tr>
</tbody>
</table>
Methodology for Radiographic Observations

• Spinous Process Fractures
  – MMI reviewed all radiographs at all time points
    • Sequential review to determine changes in spinous process with time
  – Both neutral and flexion-extension radiographs reviewed
    • Software utilized to visually stabilize vertebral body
    • Motion of fracture fragment utilized to identify fractures

• Device Migration
  – Defined as AP migration > 5mm, measured using QMA tools

• Device Dislodgement
  – Defined as superior or inferior wings are no longer in contact with bone and / or device is completely extruded
Analysis Populations

Patient Cohorts

- **Intent-to-treat (ITT):** all randomized subjects screened and scheduled for surgery with an anesthesia start time regardless of treatment received

- **Modified Intent-to-treat (mITT):** all randomized subjects with an anesthesia start time. Subjects with an anesthesia start time, but that do not receive a device, or receive the wrong device, will be failures.

- **Per protocol (PP):** all subjects with 24 month follow-up data and no major inclusion/exclusion protocol deviations and subjects that failed before 24 months and subsequently did not complete 24 months.
Statistical Analysis Plan

• Bayesian posterior design for assessing clinical non-inferiority
• Last treated patient reached month 24 follow-up 12/16/2013
• Identification of Superion® success through use of endpoints from multiple domains

• **Study success criterion:** Bayesian posterior probability for $(\pi_s - \pi_x > -0.10)$ is at least equal to **0.958**
  – 10% non-inferiority margin
  – Non-informative priors used in design phase
  – Bayesian multiple imputations performed for missing data
  – Bayesian simulations established *a priori* 0.958 threshold to satisfactorily control type I error based on the design
Study Conduct Summary

• *A priori* study design & protocol (IDE G070118)
  – Collaborative selection of appropriate control device for patient population

• Radiographic review by independent core lab (Medical Metrics, Inc.)

• Independent clinical events committee (CEC)
  – Adjudicated **all** adverse events determined by the investigator to be “Related” or of “unknown / undetermined” relationship to device, procedure, or adjacent level

• Exceptional Follow-Up and Patient Retention
Superion® ISS Study Results

Glenn Stiegman, MS
Vice President, Clinical & Regulatory Affairs
Musculoskeletal Clinical Regulatory Advisers, LLC
Subjects Consented & Randomized
n=470

- Post-Consent Screen Failures (n=51)
- Superion® Training Patients (n=28)

Randomized Cohort
n=391
(Superion®=190, X-STOP®=201)

- Randomized but lack anesthesia start time (n=0)

Modified Intent-to-Treat (mITT) Cohort n=391
(Superion®=190, X-STOP®=201)

- Protocol Violators (n=19)
- Missing 24M (n=21)

Per Protocol Cohort
n=351
(Superion®=173, X-STOP®=178)

Greater than 94% Follow-Up Rate at 24 Months for Both Arms
# Patient Demographics

## Summary of Continuous Variables at Baseline

<table>
<thead>
<tr>
<th></th>
<th>Superion®</th>
<th>X-STOP®</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery (yrs.)</td>
<td>66.9</td>
<td>66.2</td>
<td>0.522</td>
</tr>
<tr>
<td>BMI</td>
<td>29.5</td>
<td>29.7</td>
<td>0.609</td>
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</table>

## Summary of Demographic Categorical Variables

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<th>Superion®</th>
<th>X-STOP®</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>110</td>
<td>129</td>
<td>0.214</td>
</tr>
<tr>
<td>Females</td>
<td>80</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td><strong>Spondylolisthesis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 Spondylolisthesis</td>
<td>68</td>
<td>75</td>
<td>0.594</td>
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<tr>
<td>No Spondylolisthesis</td>
<td>115</td>
<td>112</td>
<td></td>
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<tr>
<td><strong>Stenosis Type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central Only</td>
<td>64</td>
<td>58</td>
<td>--</td>
</tr>
<tr>
<td>Lateral Only</td>
<td>16</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>103</td>
<td>114</td>
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</tr>
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</table>

## Summary of IntraOperative Variables

<table>
<thead>
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<th>Superion®</th>
<th>X-STOP®</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td><strong>Levels Treated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-level</td>
<td>99</td>
<td>99</td>
<td>0.613</td>
</tr>
<tr>
<td>2-level</td>
<td>90</td>
<td>100</td>
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</tbody>
</table>
Peri-Operative Results

<table>
<thead>
<tr>
<th>Operative Detail</th>
<th>Superion® IDE</th>
<th></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Superion®</td>
<td>X-STOP®</td>
<td></td>
</tr>
<tr>
<td>(n=190)</td>
<td>(n=200)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Loss (cc)</td>
<td>13.5 ± 15.9</td>
<td>38.7 ± 43.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital Length of Stay (days)</td>
<td>1.80 ± 1.5</td>
<td>1.90 ± 1.5</td>
<td>0.046</td>
</tr>
<tr>
<td>Operative Time (min)</td>
<td>56.3 ± 26.8</td>
<td>47.2 ± 18.8</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- Less blood loss in Superion® arm
- Less operative time in the X-STOP® arm
- Differences not considered clinically meaningful

Both Treatments Demonstrate Low Blood Loss and Minimal Operative Time
77.1% of Superion® & 80.5% of X-STOP® Patients Met MCID Success at 24 Mos
72.5% of Superion® & 80.5% of X-STOP® Patients Met MCID Success at 24 Mos
84.0% of Superion® & 91.7% of X-STOP® Patients Met Success Threshold at 24 Mos
Re-operations & Revisions

- No significant difference in revision rates
- Similar rates of patients had decompression and device removal
  - 13.7% Superion® vs. 11.4% X-STOP®, p = 0.543
- Higher revision rate between 24 and 36 months in X-STOP® arm

<table>
<thead>
<tr>
<th></th>
<th>Superion®</th>
<th>X-STOP®</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-ops / Revisions (24M)</td>
<td>20.0%</td>
<td>14.4%</td>
<td>0.179</td>
</tr>
<tr>
<td>Re-ops / Revisions (36M)</td>
<td>25.8%</td>
<td>21.9%</td>
<td>0.365</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary Cause of Revisions Related to Disease Symptoms, Not Complications</th>
<th>Superion®</th>
<th>X-STOP®</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of Efficacy</td>
<td>11</td>
<td>7</td>
<td>0.783</td>
</tr>
<tr>
<td>Return of Symptoms</td>
<td>5</td>
<td>4</td>
<td>1.000</td>
</tr>
<tr>
<td>Disease Progression</td>
<td>13</td>
<td>10</td>
<td>1.000</td>
</tr>
<tr>
<td>Safety</td>
<td>6</td>
<td>8</td>
<td>0.364</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>29</td>
<td>0.179</td>
</tr>
</tbody>
</table>
Additional Treatment

- Subjects who received potentially confounding treatments are considered failures
  - Epidural injections at the index level
  - Nerve root block procedures at the index level
  - Spinal cord stimulators
  - Rhizotomies

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Superion®</th>
<th>X-STOP®</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural injections or nerve block procedures at the index level(s) at any time</td>
<td>13.2%</td>
<td>16.4%</td>
<td>0.395</td>
</tr>
<tr>
<td>Spinal cord stimulators or rhizotomies</td>
<td>0</td>
<td>0.5%</td>
<td>1.000</td>
</tr>
</tbody>
</table>
Complications

Radiographic Observations Evaluated by MMI

- **Spinous Process Fracture**
  - Failure defined as non-healed fractures at 24 months

- **Device Migration**
  - Failure defined as AP migration > 5mm

- **Device Dislodgement**
  - Superior or inferior wings are no longer in contact with bone and / or device is completely extruded

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Re-operations &amp; Revisions</th>
<th>Additional Treatment</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic Failure</td>
<td>Superion®: 3.7%</td>
<td>X-STOP®: 2.5%</td>
<td></td>
</tr>
<tr>
<td>Deep Wound Infection</td>
<td>0.0%</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Device - or Procedure - Related Deaths</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Radiographic Observations</td>
<td>11.1%</td>
<td>13.9%</td>
<td></td>
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</tbody>
</table>
**Primary Endpoint: Overall Success**

<table>
<thead>
<tr>
<th>Analysis Cohort</th>
<th>Number and Percentage Achieving Month 24 Overall Success</th>
<th>Posterior Probability of Non-Inferiority</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Superion®</td>
<td>%</td>
</tr>
<tr>
<td>mITT</td>
<td>183</td>
<td>95</td>
</tr>
<tr>
<td>PP</td>
<td>173</td>
<td>92</td>
</tr>
</tbody>
</table>

- Impact of missing data is minimal
- MI informed by clinical status at earlier clinical visits and included 5000 simulations
- Only 7/190 (3.7%) Superion® and 14/201 (7.0%) X-STOP® patients missing primary Month 24 CCS

**Achieved a priori Primary Endpoint Success**
### Primary Endpoint: Component Success

<table>
<thead>
<tr>
<th>Component Success</th>
<th>Superion®</th>
<th>X-STOP®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Success (2 / 3 ZCQ Domains)</td>
<td>81.7%</td>
<td>87.2%</td>
</tr>
<tr>
<td>No Re-operations &amp; Revisions</td>
<td>80.0%</td>
<td>86.6%</td>
</tr>
<tr>
<td>No Confounding Additional Treatments</td>
<td>86.3%</td>
<td>82.6%</td>
</tr>
<tr>
<td>No Major Related Complications</td>
<td>86.8%</td>
<td>83.1%</td>
</tr>
</tbody>
</table>

**Greater than 80% Success in All Major Components For Both Groups**
Achieve Primary Endpoint

Clinical Outcomes

- Clinically significant improvement in stenosis symptoms
- Most due to lack of treatment effect or advancement of disease

Complications

- Similar rates of radiographic observations in both arms
- Slightly higher rate of injections in X-Stop® arm

Additional Treatments

Re-operations/Revisions
75.6% of Superion® & 77.4% of X-STOP® Patients Met MCID Success at 24 Mos
Secondary Clinical Outcomes

**Oswestry Disability Index**
Superion® 63.4% 24 month success  
X-STOP® 66.9% 24 month success  
p-value = 0.606

**VAS Back Pain**
Superion® 67.2% 24 month success  
X-STOP® 68.4% 24 month success  
p-value = 0.469
Radiographic Outcomes

• No difference in flexion / extension angles between Superion® and X-STOP® arms
• No difference in translation between Superion® and X-STOP® arms
• Similar distraction at 24 months
• Reduction in ROM demonstrated at 24 months

Radiographic Data and Clinical Outcomes Indicate Extension Blocking is Method of Action
Effectiveness Summary

• Superion® mITT CCS of 52.7% vs X-STOP® 50.2%
  – > 80% success in all 4 components of the primary endpoint
  – Posterior probability of non-inferiority = 0.9927
  – Met study success criterion: Bayesian posterior probability ≥ 0.958

• Improvement from baseline in all clinical outcome measures
  – Significant improvement beyond the MCID, durable to 36 months

• Radiographic data show evidence of extension blocking

Patients Achieved Consistent, Meaningful and Lasting Clinical Improvement
## Adverse Event Rates - CEC Adjudicated

<table>
<thead>
<tr>
<th>Event</th>
<th>Superion® (N=190)</th>
<th>X-STOP® (N=201)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Any adverse event (per patient)</td>
<td>180</td>
<td>94.7</td>
</tr>
<tr>
<td>Any device related AE</td>
<td>22</td>
<td>11.6</td>
</tr>
<tr>
<td>Any procedure related AE</td>
<td>27</td>
<td>14.2</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>88</td>
<td>46.3</td>
</tr>
<tr>
<td>Serious AE that is either device or procedure related</td>
<td>16</td>
<td>8.4</td>
</tr>
<tr>
<td>Deaths</td>
<td>6</td>
<td>3.2</td>
</tr>
</tbody>
</table>

- No device-related or procedure-related deaths
- Device or procedure-relation classification
  - related, not related, unknown / undetermined
- “Worst case” assessment performed
Fracture AE Reporting Compared to Core Lab

- Adverse events contribute to safety profile
  - Investigator reported spinous process fractures
  - CEC adjudicated spinous process fractures
- Only Core Lab determination contributes to CCS success
  - CCS success if healed by 24 months
  - CCS failure if fracture is present at 24 months

<table>
<thead>
<tr>
<th></th>
<th>Training Cohort</th>
<th>Superion® mITT Cohort</th>
<th>X-STOP® mITT Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Events</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Site Reported(^1)</td>
<td>0</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Post-CEC Adverse Event Review &amp; Categorization</td>
<td>3</td>
<td>24</td>
<td>14</td>
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<tr>
<td>Medical Metrics Review</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Independent Radiographic Review</td>
<td>6</td>
<td>31</td>
<td>17</td>
</tr>
<tr>
<td>Non-Healed (M24)</td>
<td>2</td>
<td>21</td>
<td>10</td>
</tr>
</tbody>
</table>

\(^1\)Site-reported fractures are those adverse events originally placed in the “spinous process fracture” category by the investigators.
Safety Summary

• Superion® provides a similar safety profile to approved X-STOP® device
  – Similar types of adverse events
  – Similar rate of adverse events

• Device & procedure related adverse events
  – Similar rates of related adverse events

• Re-operations & revisions
  – Similar rates for both Superion® and X-STOP®
82.9% of Superion® and 75.3% of X-STOP® Patients Met MCID Success at 36 Months
80.5% of Superion® and 77.9% of X-STOP® Patients Met MCID Success at 36 Months
91.5% of Superion® and 88.3% of X-STOP® Patients Met Success Threshold at 36 Months
## 36 Month Composite Clinical Success

<table>
<thead>
<tr>
<th>Analysis Cohort</th>
<th>Superion®</th>
<th>X-STOP®</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>mITT</td>
<td>120</td>
<td>63</td>
</tr>
</tbody>
</table>

- Evaluated based on primary endpoint CCS definition
- No new radiographic observations
- > 90% follow-up of theoretically due patients

**Longer Term Data Show Continued and Stable Treatment Effect for Superion®**
36 Month Secondary Endpoints

VAS Worse Leg Pain
- Superion® meeting success 84.1%
- X-STOP® meeting success 69.7%

VAS Back Pain
- Superion® meeting success 76.8%
- X-STOP® meeting success 69.7%

Superion® Patients Maintain Treatment Effect in Back and Leg Pain at 36 Months
Overall Superion® Study Conclusions

• Demonstrated reasonable assurance of safety and effectiveness

• Established clinical non-inferiority compared to control device
  – Posterior probability of 0.9927

• Demonstrated clinically significant improvement in pain & function measurements over baseline

• Maintained favorable longer term clinical outcomes

• Established positive risk-benefit profile compared to X-STOP® control device

Treatment Effect Demonstrated Through 36 Months
Radiographic Observations in the Superion® IDE

Scott Blumenthal, MD
Medical Director, VertiFlex®, Inc.
Spine Surgeon, Texas Back Institute
Clinical Assistant Professor, Orthopedic Surgery,
UT Southwestern Medical School
## Primary Radiographic Observations

<table>
<thead>
<tr>
<th>Radiographic Observation</th>
<th>Superion® (n=190)</th>
<th>X-STOP® (n=201)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Spinous Process Fracture (at any time)</td>
<td>31</td>
<td>16.3%</td>
</tr>
<tr>
<td>Spinous Process Fracture (non-healed at 24 months)</td>
<td>21</td>
<td>11.1%</td>
</tr>
<tr>
<td>Device Migration (&gt; 5mm)</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Device Dislodgement</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Any Radiographic Observation (24 months)</td>
<td>21</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

*Significant overlap was present in X-STOP® subjects having spinous process fractures, device migration, and device dislodgement.

- Fracture healing determined by MMI
- Protocol defined healed fracture as one having mature osseous bridging between fracture fragments
Comparison of SPF to Migration / Dislodgement

Superion® Radiographic Observations (N=31)

X-STOP® Radiographic Observations (N=34)

- Spinous Process Fractures (N=31)
- Device Migrations (N=13)
- Device Dislodgements (N=20)
Radiographic Observation Assessment

1. Provide characterization of radiographic observations
   - Time course and healing
   - Location
   - Displacement

2. Evaluate clinical outcomes
   - Effect on pain and function
   - Effect on additional treatment rates

3. Investigate potential risk factors
   - Demographic
   - Anatomic
   - Device placement
## Time Course of Spinous Process Fracture

<table>
<thead>
<tr>
<th></th>
<th>Post-op - Week 6</th>
<th>Month 3 - 12 Months</th>
<th>Month 18 - Month 24</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superion®</td>
<td>27</td>
<td>4</td>
<td>-</td>
<td>31</td>
</tr>
<tr>
<td>X-STOP®</td>
<td>14</td>
<td>3</td>
<td>-</td>
<td>17</td>
</tr>
<tr>
<td>Superion®</td>
<td>87.1%</td>
<td>12.9%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>X-STOP®</td>
<td>82.4%</td>
<td>17.6%</td>
<td>0.0%</td>
<td></td>
</tr>
</tbody>
</table>

- No additional fracture observations after 12 months

### Majority of Fractures Occurred Acutely in Both Arms
Spinous Process Fracture Characterization

- Majority of Superion® fractures coincident with device (80.6%)
- Majority of X-STOP® fractures anterior to device (70.6%)
- Majority of all fractures displaced > 2mm
32.3% of Superion® and 41.2% of X-STOP® Fractures Healed Prior to 24 Months
32.3% of Superion® and 41.2% of X-STOP® Fractures Healed Prior to 24 Months
32.3% of Superion® and 41.2% of X-STOP® Fractures Healed Prior to 24 Months
Characterization of X-STOP® Dislodgement / Migration

- 30% complete dislodgement
- Mean migration displacement of 8.4 ± 3.3 mm
- 62.5% occurred acutely (within 6 weeks)
Fracture Characterization Summary

• Occurred acutely

• Fracture location
  – Majority of Superion® coincident to device
  – Majority of X-STOP® anterior to device

• Fracture Healing
  – 32.3% fracture healing in Superion®
  – 41.2% fracture healing in X-STOP®

• Many X-STOP® fractures exhibited secondary migration & dislodgement
1. Provide characterization of radiographic observations
   – Time course and healing
   – Location
   – Displacement

2. Evaluate clinical outcomes
   – Effect on pain and function
   – Effect on additional treatment rates

3. Investigate potential risk factors
   – Demographic
   – Anatomic
   – Device placement
Radiographic Observations: ZCQ Outcomes

Superion® mITT Population (24 Months)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Radiographic Observation</th>
<th>No Radiographic Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZCQ PF</td>
<td>73.9%</td>
<td>72.2%</td>
</tr>
<tr>
<td>ZCQ SS</td>
<td>78.3%</td>
<td>76.9%</td>
</tr>
<tr>
<td>ZCQ PS</td>
<td>73.9%</td>
<td>86.1%</td>
</tr>
</tbody>
</table>

X-STOP® mITT Population (24 Months)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Radiographic Observation</th>
<th>No Radiographic Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZCQ PF</td>
<td>80.8%</td>
<td>80.4%</td>
</tr>
<tr>
<td>ZCQ SS</td>
<td>76.9%</td>
<td>81.3%</td>
</tr>
<tr>
<td>ZCQ PS</td>
<td>88.5%</td>
<td>92.5%</td>
</tr>
</tbody>
</table>

No Clinical Effect of Radiographic Observations
Radiographic Observations: Pain Outcomes

Superion® mITT Population (24 Months)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>With Radiographic Observation</th>
<th>Without Radiographic Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODI</td>
<td>65.2%</td>
<td>63.0%</td>
</tr>
<tr>
<td>VAS Back</td>
<td>78.3%</td>
<td>64.8%</td>
</tr>
<tr>
<td>VAS Leg (Worse)</td>
<td>73.9%</td>
<td>75.9%</td>
</tr>
</tbody>
</table>

X-STOP® mITT Population (24 Months)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>With Radiographic Observation</th>
<th>Without Radiographic Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODI</td>
<td>65.4%</td>
<td>67.3%</td>
</tr>
<tr>
<td>VAS Back</td>
<td>50.0%</td>
<td>72.9%</td>
</tr>
<tr>
<td>VAS Leg (Worse)</td>
<td>69.2%</td>
<td>79.4%</td>
</tr>
</tbody>
</table>

*No Clinical Effect of Radiographic Observations in Superion® Patients*

*p-value = 0.034*
Fractures: ZCQ Outcomes

Superion® mITT Population (24 Months)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Fracture Patients</th>
<th>Non-Fracture Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZCQ PF</td>
<td>73.9%</td>
<td>72.2%</td>
</tr>
<tr>
<td>ZCQ SS</td>
<td>78.3%</td>
<td>76.9%</td>
</tr>
<tr>
<td>ZCQ PS</td>
<td>73.9%</td>
<td>86.1%</td>
</tr>
</tbody>
</table>

X-STOP® mITT Population (24 Months)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Fracture Patients</th>
<th>Non-Fracture Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZCQ PF</td>
<td>76.9%</td>
<td>80.8%</td>
</tr>
<tr>
<td>ZCQ SS</td>
<td>69.2%</td>
<td>81.7%</td>
</tr>
<tr>
<td>ZCQ PS</td>
<td>84.6%</td>
<td>92.5%</td>
</tr>
</tbody>
</table>

No Clinical Effect of Fractures in Superion® Patients
Fractures: Pain Outcomes

Superion® mITT Population (24 Months)

- **ODI**: Fracture Patients 65.2%, Non-Fracture Patients 63.0%
- **VAS Back**: Fracture Patients 78.3%, Non-Fracture Patients 64.8%
- **VAS Leg (Worse)**: Fracture Patients 73.9%, Non-Fracture Patients 75.9%

X-STOP® mITT Population (24 Months)

- **ODI**: Fracture Patients 61.5%, Non-Fracture Patients 67.5%
- **VAS Back**: Fracture Patients 46.2%, Non-Fracture Patients 70.8%
- **VAS Leg (Worse)**: Fracture Patients 69.2%, Non-Fracture Patients 78.3%

**No Clinical Effect of Fractures in Superion® Patients**
Significantly Greater VAS Back Pain Associated with Dislodgements & Migrations

X-STOP® mITT Population (24 Months)

- **Dislodgement or Migration**
- **No Dislodgement or Migration**

*Significance indicated by *p*-value = 0.014
### Additional Treatments

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th><strong>Superion®</strong></th>
<th></th>
<th><strong>X-STOP®</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radiographic Observation</td>
<td>No Radiographic Observation</td>
<td>Radiographic Observation</td>
<td>No Radiographic Observation</td>
</tr>
<tr>
<td>Reoperation or Revision</td>
<td>12.9% (4/31)</td>
<td>21.4% (34/159)</td>
<td>14.7% (3/34)</td>
<td>14.4% (24/167)</td>
</tr>
<tr>
<td>Epidural Steroid Injection or Nerve Root Block</td>
<td>12.9% (4/31)</td>
<td>13.2% (21/159)</td>
<td>8.8% (3/34)</td>
<td>18.0% (30/167)</td>
</tr>
<tr>
<td>Overall Additional Treatment</td>
<td>19.4% (6/31)</td>
<td>27.7% (44/159)</td>
<td>20.6% (7/34)</td>
<td>28.7% (48/167)</td>
</tr>
</tbody>
</table>

**Note:** Radiographic Observations Did Not Result in a Greater Number of Additional Treatments.
Biomechanical Support

- Primary mechanism of action = Extension Blocking
  - ROM Data (Flexion to Extension) utilized to show extension blocking
  - Limitations with use of neutral to extension

Changes from Pre-Op in Range of Motion (F to E)

<table>
<thead>
<tr>
<th>Device</th>
<th>Fracture Effect</th>
<th>No Fracture Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superion®</td>
<td>19.3% ↓ in ROM</td>
<td>26.3% ↓ in ROM @ 24 M</td>
</tr>
<tr>
<td>X-STOP®</td>
<td>7.4% ↑ in ROM</td>
<td>19.3% ↓ in ROM @ 24 M</td>
</tr>
</tbody>
</table>

- Fracture:
  - Superion®: 21.1% ↓ in ROM
  - X-STOP®: 22.1% ↓ in ROM

- No Fracture:
  - Superion®: 27.5% ↓ in ROM
  - X-STOP®: 19.3% ↓ in ROM

Superion® Maintained Mechanism of Action Even With Spinous Process Fracture
Clinical Outcome Summary

• Similar clinical results with and without fracture in the Superion® arm
  – No effect on patient pain and function
  – No effect on additional treatment rates

• Statistically significant difference in VAS-Back Pain in the X-STOP® group
  – Increase in VAS-Back Pain primarily seen in X-STOP® patients with migrations & dislodgements

• Mechanism of action preserved due to
  – Superion® placement
  – Coincident fracture location
Radiographic Observation Assessment

1. Provide characterization of radiographic observations
   - Time course and healing
   - Location
   - Displacement

2. Evaluate clinical outcomes
   - Effect on pain and function
   - Effect on additional treatment rates

3. Investigate potential risk factors
   - Demographic
   - Anatomic
   - Device placement
Investigation of Demographic Risk Factors

• No correlation in fracture incidence to most demographic factors
  – Only correlation in Superion®
    • Age < 67 years - Odds Ratio: 1.73
    • BMI ≥ 29.5 - Odds Ratio: 2.20
    • Odds ratio skewed toward BMI >35

• No correlation in migration & dislodgement incidence to most demographic factors
  – Correlation in X-STOP
    • Age < 67 - Odds Ratio: 1.72
    • BMI ≥ 29.5 - Odds Ratio: 2.49

No Unexpected Demographic Trends


### Investigation of Anatomical Risk Factors

- **L4 Spinous Process Height (< 21mm)**
  - Superion® fracture - Odds Ratio: 2.15
  - X-STOP® fracture - Odds Ratio: 3.15

- **Kissing Spinous Processes**
  - Superion® fracture - Odds Ratio: 1.59
  - X-STOP® fracture - Odds Ratio: 1.83

- **Grade 1 Spondylolisthesis vs without Spondylolisthesis**
  - Superion® fracture - Odds Ratio 1.26
  - X-STOP® fracture - Odds Ratio 1.44
### Potential Intraoperative Risk Factors

- **Shallow placement**: 4 times more likely to result in fracture
- **Nominal increase in fracture rate in 2 level patients when compared to 1 level patients**

#### Shallow Placement Will Be Mitigated Through Surgeon Training

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Superion® Odds of Fracture</th>
<th>X-STOP® Odds of Fracture</th>
<th>Odds of Migration / Dislodgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shallow vs Not Shallow</td>
<td>4.2</td>
<td>4.0</td>
<td>3.2</td>
</tr>
<tr>
<td>2 Level vs 1 Level</td>
<td>1.6</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>1 Level vs 2 Level</td>
<td></td>
<td></td>
<td>1.4</td>
</tr>
</tbody>
</table>
Summary of Radiographic Risk

• Primary spinous process fracture risk factors
  – Shallow placement
  – Height of spinous processes
• Similar risk factors for fracture and migration / dislodgement
• Radiographic observation risk mitigated by training and labeling
  – Proper sensitivity to patient features
  – Exercise particular care in placement technique

Spinous Process Fracture Risk Not Correlated to Clinical Outcomes
Risk / Benefit Profile

Pierce D. Nunley, MD
Study Investigator, Superion® Trial
Associate Professor, LSUHSC
Director, Spine Institute of Louisiana
• Superion® indicated to treat moderate spinal stenosis
  – Demonstrated clinical benefit through 24 & 36 months
  – Continued reduction in range of motion → evidence of extension blocking
  – Less invasive posterior surgical approach preserves surrounding anatomy
  – No demonstrated risk of device migration & dislodgement compared with X-STOP®

Superion® Is a Valid Option for the Treatment of Moderate Stenosis
Risk Profile Compared to X-STOP®

- Similar risk profile to X-STOP®
  - Adverse event profile similar to X-STOP®
    - Similar rates of device- and procedure-related adverse events
    - Similarly low serious adverse event rates
- Radiographic observations
  - Slightly higher rates of spinous process fractures
  - No migrations or dislodgements

Risk Mitigated by Surgeon Training & Labeling
Risk of Spinous Process Fracture

- Risk of fracture demonstrated for posterior devices
- FDA referenced several articles that reported fractures
  - Articles lack quality comparative data
  - Low sample size
  - Single arm
  - Dissimilar patient population
  - Off-label use

Best Means of Comparison - Level 1 Clinical Evidence
Limitations in Fracture Literature Cited by FDA

  - 23% spinous process fracture rate
  - Non-indicated patient population (severe stenosis): 69% of patients

- Kim et al. (2011): Single-Arm Study of 38 Subjects
  - 28.9% spinous process fracture rate (CT performed on all patients)
  - 11.2% symptomatic spinous process fracture rate
  - Multiple devices (X-STOP® & Lanx Aspen)

  - 5.8% spinous process fracture rate, 75% required revision
  - Mixed patient population (Stenosis and/or facet joint syndrome)

- Moojen et al. (2015): coflex® without decompression vs decompression
  - 4.3% spinous process fracture rate
  - Use inconsistent with US approval

Small Scale Investigations, Variable Results
Level I Clinical Evidence

- Two Level I Clinical Studies of Interspinous Devices
  - Superion® IDE: 391 mITT Subjects, moderate stenosis
  - coflex® IDE: 322 Per Protocol Subjects, moderate/severe stenosis, in conjunction with direct decompression
- Both studies used same radiographic core laboratory (MMI)
- coflex® IDE reported 75% of spinous process fractures were asymptomatic

<table>
<thead>
<tr>
<th>Device</th>
<th>Fracture Rate</th>
<th>Healing Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superion® (n=190)</td>
<td>16.3%</td>
<td>32%</td>
</tr>
<tr>
<td>X-STOP® (n=201)</td>
<td>8.5%</td>
<td>41%</td>
</tr>
<tr>
<td>coflex® (n=215)</td>
<td>14.0%</td>
<td>48%</td>
</tr>
<tr>
<td>Posterolateral Fusion (n=107)</td>
<td>11.9%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Level I Data Demonstrate Lack of Clinical Sequelae Associated with Spinous Process Fractures
Benefit / Risk Profile Compared to Treatment Alternatives

• Relative efficacy
  – Real-world success based on leg pain relief
  – Comparable improvement versus direct decompression

• Perioperative metrics
  – More favorable versus other surgical options

• Postoperative complications
  – Fewer and less significant procedure-related complications

• Re-operations and revisions
  – Indirect decompression does not limit future surgical options
  – Re-operations treat disease symptoms, not safety driven

Interspinous Spacer Benefit / Risk Profile
Supported by Level I Clinical Data
Comparative Effectiveness of Treatment Options

Leg Pain Severity Improvement at 2 Years with LSS Therapies

Less Invasive

<table>
<thead>
<tr>
<th>Author (Journal)</th>
<th>n</th>
<th>Final PMA Trial Results</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manchikanti (Pain Physician 2012)</td>
<td>50</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Davis (Spine 2013)</td>
<td>86</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>Stromqvist (Spine 2013)</td>
<td>50</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td>Malmivvaara (Spine 2007)</td>
<td>42</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>Haro (Spine 2008)</td>
<td>50</td>
<td>76%</td>
<td></td>
</tr>
</tbody>
</table>

More Invasive

<table>
<thead>
<tr>
<th>Author (Journal)</th>
<th>n</th>
<th>Surgical Laminectomy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis (Spine 2013)</td>
<td>86</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>Stromqvist (Spine 2013)</td>
<td>50</td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>Malmivvaara (Spine 2007)</td>
<td>42</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>Haro (Spine 2008)</td>
<td>50</td>
<td>76%</td>
<td></td>
</tr>
</tbody>
</table>
Comparative Effectiveness of Treatment Options

- **Superion®**: Final PMA Results, n=126
- **Decompression**: Stromqvist et al., Spine 2013, n=50
- **Decompression**: Lonne et al., Spine 2015, n=41
- **Fusion**: Davis et al., Spine 2013, n=86
## Major Benefit of Indirect Decompression: Perioperative Outcomes

<table>
<thead>
<tr>
<th>Operative Detail</th>
<th>Superion® IDE</th>
<th>coflex® IDE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Superion®</td>
<td>X-STOP®</td>
</tr>
<tr>
<td></td>
<td>(n=190)</td>
<td>(n=201)</td>
</tr>
<tr>
<td>Operative Time (min)</td>
<td>56.3 ± 26.8</td>
<td>47.2 ± 18.8</td>
</tr>
<tr>
<td>Blood Loss (cc)</td>
<td>13.5 ± 15.9</td>
<td>38.7 ± 43.8</td>
</tr>
<tr>
<td>Hospital Length of Stay (days)</td>
<td>1.80 ± 1.5</td>
<td>1.90 ± 1.5</td>
</tr>
</tbody>
</table>

**Indirect Decompression Associated With More Favorable Perioperative Metrics**
### Medicare Data Show Lower Complication and Lower Early Re-hospitalization Rates in Patients Treated with Interspinous Process Spacers*

<table>
<thead>
<tr>
<th></th>
<th>Interspinous Process Spacer</th>
<th>Decompression Alone</th>
<th>Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size (N)</td>
<td>3,912</td>
<td>75,310</td>
<td>16,623</td>
</tr>
<tr>
<td>Early Wound Complications</td>
<td>0.8%</td>
<td>1.8%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Early Cardiopulmonary/Stroke</td>
<td>1.0%</td>
<td>1.6%</td>
<td>2.9%</td>
</tr>
<tr>
<td>All-cause early re-hospitalization</td>
<td>4.5%</td>
<td>6.6%</td>
<td>9.4%</td>
</tr>
</tbody>
</table>


### Superion® Associated With Fewer Post-operative Complications (e.g., nerve injury, dural tear, deep infection, epidural fibrosis)
Scientific Basis for Comparison of Treatments

- FDA has pointed to several articles evaluating decompression compared with interspinous process devices

<table>
<thead>
<tr>
<th>Reference</th>
<th>Issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moojen 2015, 2013</td>
<td>• Poor quality of peer review</td>
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<tr>
<td></td>
<td>• Device use inconsistent with US approved indications (coflex without decompression)</td>
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<tr>
<td>Moojen 2014</td>
<td>• Editorial (i.e., not original research)</td>
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<tr>
<td>Epstein 2012</td>
<td>• Poor quality of peer review</td>
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<tr>
<td></td>
<td>• Low level of evidence (summary of papers)</td>
</tr>
<tr>
<td>Kabir 2010</td>
<td>• Summary of papers on IPD</td>
</tr>
<tr>
<td></td>
<td>• Statement of “controversial” use of ISP with spondylolisthesis lacks data support</td>
</tr>
<tr>
<td>Stromqvist 2013</td>
<td>• Reoperation rates skewed by outlier site</td>
</tr>
</tbody>
</table>

Lack of Quality Comparative Data
Indirect Decompression Re-Operation Rate and Options

Indirect Decompression

Success (>80%)

Ineffective (<20%)

Virgin Decompression

Virgin Decompression + Fusion

Should Be Considered a First Line Option for the Moderate Stenosis Patient
Direct Decompression Re-Operation Rate and Options

Decompression Sequelae:

- **Complication rate:** 7-9%\(^3,4,5,6\)
- **Readmission rate:** 8-10% per year\(^7\)
- **Reoperation rate:** 17%\(^4,8\)

Summary of Benefits and Risks

• Benefits of Superion®
  – Less invasive approach
  – Fewer post-operative complications
  – Demonstrates clinical benefit through 24 & 36 months

• Risks
  – Re-operation rate (80% of patients did not require re-operation)
  – Spinous process fracture (majority asymptomatic, 32% healing rate)

• Risk Mitigation
  – Labeling modifications proposed to mitigate risks
  – Surgeon training to optimize patient selection and device placement
  – Continued investigation in post approval studies
Post-Approval Study Considerations

• Study I: Long-term Follow-Up
  – Follow IDE subjects to 5 years
  – Continued collection of IDE data
  – FDA proposed use of CT scans for fracture patients

• Study II: Actual Conditions of Use
  – FDA proposed decompression control
  – FDA proposed 2 year CCS evaluation with 3 year longer-term follow-up
  – FDA proposed use of CT scans for radiographic observations

Actual Conditions of Use Study Intended to Validate Risk Mitigation Measures
Closing Remarks

Earl R. Fender
President & CEO
VertiFlex®, Inc.
Overall Conclusions

- Substantiated trial design
- Addressed radiographic observations
- Proved safety, effectiveness & positive benefit / risk
Superion® Interspinous Spacer
Panel Meeting
P140004

February 20, 2015