These two components are packaged together and are physically combined immediately after dilution with sterile saline. The rhPDGF-BB functions as a chemo-attractant and mitogen for cells involved in bone generation and fracture healing. The LBS054-01 Augment® Bone Graft is a combination device/drug product for use in bone repair and fracture healing.

I. DEVICE DESCRIPTION

A. Augment® Bone Graft

Augment® Bone Graft is a combination of TCP, a bioactive glass material, and rhPDGF-BB, a recombinant human platelet-derived growth factor-BB. The TCP is a non-resorbable, osteoconductive bone graft substitute, and the rhPDGF-BB is a recombinant protein that enhances bone regeneration.

B. RhPDGF-BB

rhPDGF-BB is a protein that promotes the migration and proliferation of various cell types involved in bone regeneration, including mesenchymal stem cells and osteoblasts. It is a biologically active component of the Augment® Bone Graft.

C. Augment® Bone Graft vs. Autograft

Augment® Bone Graft can be used as an alternative to autograft, which is a bone graft taken from the patient's own body. Augment® Bone Graft offers several advantages compared to autograft, including reduced donor site morbidity, decreased surgical time, and improved clinical outcomes.

D. Study Population

The study population consisted of 397 patients (414 patients in the Safety, or "All Treated", group minus an unspecified number of patients who did not receive Augment® Bone Graft). The patients were divided into two groups: Augment® Bone Graft group and autograft control group.

E. Indicating Need for Graft Material

The following factors were considered when determining the need for graft material:

- At least one joint to be fused
- More than one joint to be fused
- Evidence of potential incongruous apposition
- Convexity/concavity mismatch of the articulating surfaces
- Foot Function Index (FFI) Total score above 31.5
- Need for bone graft due to pre-existing conditions

F. Table 1: Demographic & Clinical Characteristics at Baseline – "All Treated" Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Augment® Bone Graft</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G. Table 2: Radiographic Assessment of the Need for Graft Material

<table>
<thead>
<tr>
<th>Radiologic Parameter</th>
<th>Augment® Bone Graft</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parameter 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parameter 3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

H. Table 3: Vascular Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Augment® Bone Graft</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular event 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular event 2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I. Table 4: Infection Rates

<table>
<thead>
<tr>
<th>Infection</th>
<th>Augment® Bone Graft</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection 2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

J. Table 5: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Cancer

- Cancer events reported in patients who received Augment® Bone Graft: prostate (2), breast (1), hyperplastic colon (1), thyroid (1)
- Cancer events reported in patients who received autograft: prostate (2), breast (1), thyroid (1)
- Cancer events reported in patients who received placebo: prostate (2), breast (1), thyroid (1)

K. Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Cancer Mortality

- No cancer mortality events reported in patients who received Augment® Bone Graft
- One cancer mortality event reported in patients who received autograft
- One cancer mortality event reported in patients who received placebo

L. Table 6: Other Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Augment® Bone Graft</th>
<th>Autograft</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factor 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factor 3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

M. Table 7: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Immune System

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

N. Table 8: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Gastrointestinal

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

O. Table 9: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Nervous System

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

P. Table 10: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Endocrine Disorders

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

Q. Table 11: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Renal and Urinary Disorders

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

R. Table 12: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Reproductive System

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

S. Table 13: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Gastrointestinal Infestations

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

T. Table 14: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding Infections and Infections and Infestations

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

U. Table 15: Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding General Adverse Events

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

V. Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding System Organ Class

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

W. Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding MedDRA System Organ Class

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

X. Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding all MedDRA System Organ Class

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

Y. Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding all MedDRA System Organ Class

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

Z. Summary of the Three REGRANEX® Post-Approval Studies’ Findings Regarding all MedDRA System Organ Class

- No adverse events reported in patients who received Augment® Bone Graft
- Adverse events reported in patients who received autograft
- Adverse events reported in patients who received placebo

**Note:** The summaries above are based on the findings from the three REGRANEX® Post-Approval Studies and are presented in a general format. The actual data and statistical analyses are provided in the respective study reports.
did not indicate an elevated risk of cancer mortality. This study provided no evidence of a cancer risk among becaplermin users, and

Foot Function Index (FFI) Graph 4 displays data on functional improvement measured by the Foot Function Index in function according to AOFAS scores. The vast majority of subjects in both treatment groups generated to the rhPDGF-BB component of Augment® Bone Graft. The immune response to

• possible gender bias, and

SF-12 Physical Component Score

Table 7 presents data in the “Per Protocol” population. In accordance with the protocol, additional serum measurements were performed to test the stored serum samples of the pivotal study subjects who tested positive for presence of neutralizing antibodies was transient. None of those seven subjects had any activity at a single visit. All subjects returned to baseline levels at the next visits. Therefore the

improvement in, foot function as compared to baseline levels at each time point.

Because the radiographic review was inconclusive, effectiveness of Augment® Bone Graft as compared to baseline was determined as clinically significant improvement with a change in VAS of -10 to 10 mm. The analysis demonstrated equivalent improvements in outcomes for both treatment groups, with a greater incidence of post-treatment cancer, but patients treated with 3 or more tubes of REGRANEX® did not indicate an elevated risk of cancer mortality.

Graph 3 displays pain on weight bearing data (measured by VAS) at week 24 as assessed in the cohort used to determine individual success and taking into account the 2:1 randomization. Table 5 displays pain at fusion site (measured by VAS) at week 24 and week 52. In the data presentations, the “clinically significant improvement” group was defined by a greater

1 Clinically significant improvement: ≥20 mm decrease from baseline

2 Marked improvement

3 Maintained

4 Deteriorated: >10 mm increase from baseline

5 Minimal improvement

Table 5: AOFAS Hindfoot and Ankle Score at 24 and 52 Weeks – “Per Protocol” Population

<table>
<thead>
<tr>
<th>Effectiveness Results</th>
<th>Augment® Bone Graft</th>
<th>Autologous BG</th>
<th>K200-060-00</th>
<th>K200-090-00</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Subjects</td>
<td>144/223</td>
<td>12/241</td>
<td>106/132</td>
<td>10/132</td>
</tr>
<tr>
<td>1 Clinically significant improvement</td>
<td>64.6%</td>
<td>12.4%</td>
<td>67.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>2 Marked improvement</td>
<td>190/249</td>
<td>10/132</td>
<td>106/132</td>
<td>10/132</td>
</tr>
<tr>
<td>3 Maintained</td>
<td>20/80</td>
<td>0/0</td>
<td>20/80</td>
<td>0/0</td>
</tr>
<tr>
<td>4 Deteriorated</td>
<td>12/241</td>
<td>12/241</td>
<td>10/132</td>
<td>10/132</td>
</tr>
<tr>
<td>5 Minimal improvement</td>
<td>20/80</td>
<td>0/0</td>
<td>20/80</td>
<td>0/0</td>
</tr>
</tbody>
</table>

The vast majority of subjects in both treatment groups experienced an improvement in pain on weight bearing according to VAS. The vast majority of subjects in both treatment groups experienced an improvement in, foot function as compared to baseline levels at each time point.

Table 7: SF-12 Physical Component Score (PCS) at 24 and 52 Weeks – “Per Protocol” Population

<table>
<thead>
<tr>
<th>Effectiveness Results</th>
<th>Augment® Bone Graft</th>
<th>Autologous BG</th>
<th>K200-060-00</th>
<th>K200-090-00</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Subjects</td>
<td>12/117</td>
<td>87/117</td>
<td>117/132</td>
<td>4/118</td>
</tr>
<tr>
<td>1 Clinically significant improvement</td>
<td>61.7%</td>
<td>2.8%</td>
<td>80.5%</td>
<td>14.3%</td>
</tr>
<tr>
<td>2 Marked improvement</td>
<td>19/215</td>
<td>9/118</td>
<td>117/132</td>
<td>4/118</td>
</tr>
<tr>
<td>3 Maintained</td>
<td>20/80</td>
<td>0/0</td>
<td>20/80</td>
<td>0/0</td>
</tr>
<tr>
<td>4 Deteriorated</td>
<td>12/241</td>
<td>64.6%</td>
<td>12/241</td>
<td>2.8%</td>
</tr>
<tr>
<td>5 Minimal improvement</td>
<td>20/80</td>
<td>0/0</td>
<td>20/80</td>
<td>0/0</td>
</tr>
</tbody>
</table>

One way to harvest autograft provides additional benefit to patients receiving Augment® Bone Graft. Of these assessments, FDA chose to analyze VAS on weight bearing, FFI, and AOFAS in a manner. The analysis demonstrated equivalent improvements in outcomes for both treatment groups, with a greater incidence of post-treatment cancer, but patients treated with 3 or more tubes of REGRANEX® did not indicate an elevated risk of cancer mortality. This product is covered by US patent No. 7,473,678. Other patents pending.