GEM 21S®
growth-factor enhanced matrix

Regeneration like no other
GEM 21S® Growth-factor Enhanced Matrix was developed utilizing innovative tissue engineering principles which combine a bioactive protein (highly purified recombinant human platelet-derived growth factor, rhPDGF-BB) with an osteoconductive matrix (beta tricalcium phosphate, β-TCP).

This completely synthetic grafting system is engineered to stimulate wound healing and bone regeneration when implanted in the body by triggering a cascade of molecular events that continues on even after the implanted PDGF is gone. Following release at the wound site, PDGF stimulates:

- **Chemotaxis** - directed cell migration
- **Mitogenesis** - bone and periodontal ligament cell proliferation
- **Matrix formation** - e.g. collagen for new tissue formation
- **Angiogenesis** - revascularization of the surgical site

**Regeneration Like No Other**

GEM 21S® Growth-factor Enhanced Matrix promotes regeneration of bone, cementum and periodontal ligament like no other therapy available.

**Nature’s Wound Healing Agent**

GEM 21S® is the only dental therapy containing PDGF, one of the main growth factors found in the human body and well known for its role in wound healing. PDGF exerts its effects through the recruitment and stimulation of cells within the surrounding tissues.

**Powerful Stimulant**

An adequate blood supply is critical to the success of any grafting procedure. Extensive *in vitro* and *in vivo* studies have demonstrated that PDGF-BB is a powerful stimulant of angiogenesis that also stabilizes newly formed blood vessels.

**More Potent than PRP or PRGF**

GEM 21S® contains at least 1,000 times more active growth factor than either PRP or PRGF preparations.¹ ² ³ ⁴

“PDGF significantly increases the proliferation and migration of osteoblasts and other cells of the periodontum” ⁵ ⁶ ⁷
**Mechanism of Action**

The mechanism of action of PDGF is well understood. Extensive *in vitro* and animal studies have demonstrated that PDGF is a broad acting growth factor with mitogenic (cell proliferation) and chemotactic (cell recruitment) effects on osteoblasts, cementoblasts and periodontal ligament cells.

1. PDGF is released from the β-TCP matrix into the surrounding environment. PDGF then binds to specific cell surface receptors on target cells, initiating a cascade of intracellular signaling pathways.

2. PDGF-induced intracellular events lead to directed cell migration (chemotaxis) and cell proliferation (mitogenesis) of osteoblasts, periodontal ligament fibroblasts and cementoblasts.*

3. Proliferation of osteoblasts, periodontal ligament fibroblasts and cementoblasts leads to increased matrix synthesis, resulting in formation of new alveolar bone, periodontal ligament and cementum.* Angiogenesis (blood vessel formation) continues.

4. Clinical data suggests that over time (approximately 6 months), maturation of supporting alveolar bone, cementum, and periodontal ligament occurs. The end result is enhanced bone and periodontal regeneration and retention of the natural tooth.

*Based on *in-vitro* and *in-vivo* data; see device description in package insert on page 14 & 15 for complete information.
Intrabony Defects

Clinical Performance — Pivotal Trial Data
GEM 21S® is a predictable treatment for moderate to severe periodontal defects allowing clinicians the ability to retain patients’ natural teeth with confidence. In the 180 patient trial that served as the basis for FDA approval, 77% of the defects treated were difficult-to-treat 1- and 2-wall intrabony defects. Within six months, GEM 21S® significantly improved radiographic percent bone fill as compared to β-TCP alone even in the most challenging defects.*

Radiographic Percent Bone Fill by Defect Type

1-2 Wall Defects

<table>
<thead>
<tr>
<th></th>
<th>GEM 21S®</th>
<th>β-TCP Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % Bone Fill</td>
<td>53 (n=46)</td>
<td>17 (n=42)</td>
</tr>
</tbody>
</table>

p < 0.001

3 Wall and Circumferential

<table>
<thead>
<tr>
<th></th>
<th>GEM 21S®</th>
<th>β-TCP Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % Bone Fill</td>
<td>65 (n=14)</td>
<td>21 (n=14)</td>
</tr>
</tbody>
</table>

p < 0.001

Chronic smoking often significantly compromises periodontal treatment outcomes.* In the pivotal clinical trial, despite smoking up to 1 pack per day, patients treated with GEM 21S® realized significant improvement over those treated with β-TCP alone.

Radiographic Percent Bone Fill by Patient Group

Nonsmokers

<table>
<thead>
<tr>
<th></th>
<th>GEM 21S®</th>
<th>β-TCP Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % Bone Fill</td>
<td>60 (n=48)</td>
<td>16 (n=45)</td>
</tr>
</tbody>
</table>

p < 0.001

Smokers

<table>
<thead>
<tr>
<th></th>
<th>GEM 21S®</th>
<th>β-TCP Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % Bone Fill</td>
<td>39 (n=12)</td>
<td>25 (n=11)</td>
</tr>
</tbody>
</table>

p < 0.001

*See Important Safety Information on back cover.
Representative Case from the Pivotal Trial by Dr. Mark Gutt

Baseline: 9 mm deep, 1-2-walled defect between teeth #10 and #11

Nine months after treatment with GEM 21S® plus a collagen membrane

Patient presents with a poor long-term prognosis of tooth #11.

Treatment with GEM 21S® allowed the patient to retain natural dentition and provided a favorable long-term prognosis.

Representative Case from the Pivotal Trial by Dr. Michael McGuire

Baseline 9 mm probing depth and 8 mm deep by 3 mm wide, 2-wall intrabony defect

GEM 21S® in place

6 months post-op: 3 mm probing depth is observed

Pre-op radiograph

6 month post-op radiograph: increased radiopacity on the distal surface of the root

12 month post-op radiograph

36 month post-op radiograph suggests evidence of further consolidation of bone graft and increasing fill if the furcation.

Representative Case from the Pivotal Trial by Dr. Brad McAllister

Baseline: 5 mm deep, 3 mm wide, 2-wall intrabony defect

Defect treated with GEM 21S®

24 month post-op: regeneration of buccal plate across root prominence and complete fill of interproximal defect

Baseline radiograph

6 month post-op radiograph

12 month post-op radiograph

36 month post-op radiograph: normal bone trabecular pattern on the mesial and distal surfaces of the tooth
Gingival Recession Defects

Clinical Performance
A recently published randomized controlled clinical trial compared GEM 21S® Growth-factor Enhanced Matrix to Subepithelial Connective Tissue Grafts (CTG).* Investigators concluded that both the CTG and GEM 21S® treatments resulted in clinically significant improvements over the six month evaluation periods and were effective treatments for the correction of recession defects.9

### Root Coverage

<table>
<thead>
<tr>
<th></th>
<th>GEM 21S®</th>
<th>CTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % Root Coverage</td>
<td>90.8 n=30</td>
<td>98.6 n=30</td>
</tr>
</tbody>
</table>

\( p = 0.013^* \)

### Clinical Attachment Level

<table>
<thead>
<tr>
<th></th>
<th>GEM 21S®</th>
<th>CTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Change in CAL (mm)</td>
<td>1.8 n=30</td>
<td>1.7 n=30</td>
</tr>
</tbody>
</table>

\( p = 0.335^* \)

### Six Month Results
GEM 21S® treatment was statistically equivalent to CTG in the following parameters:
- Patient Satisfaction
- Esthetic Results
- Increased Keratinized Tissue

### Patient Satisfaction
At the conclusion of the trial, patients who were in need of additional surgery unanimously stated that they would prefer treatment with GEM 21S® over a CTG because they were satisfied with the esthetic results and could avoid the harvesting of a palatal graft.

*Results obtained in this trial are based on a technique that includes methods not included in approved insert. See Full Prescribing Information on page 14 & 15.
Histologic Evidence of True Periodontal Regeneration

Sites treated with GEM 21S® Growth-factor Enhanced Matrix consistently led to the formation of cementum with inserting connective tissue fibers and supporting alveolar bone. None of the CTG treated sites yielded evidence of periodontal regeneration.\textsuperscript{10, *}

Representative case of site treated with GEM 21S®

(Left) Nine months after treatment with GEM 21S®, dense cortical bone has regenerated covering the reference notch that had been placed at the presurgical osseous crest. The bone level is now just apical to the gingival reference notch (GN). ROC = regenerated osseous crest. (Right) In this ground section, both new bone and PDL have formed almost to the gingival reference notch confirming the micro CT findings.

At higher power, perpendicularly oriented connective tissue fibers are seen inserting into the newly formed bone (NB) and cellular cementum (NC). PDL = periodontal ligament.

In this low power image, newly formed cementum, PDL, and bone are observed 9 months after treatment with GEM 21S®. Note the clear demarcation between the old bone and the newly formed bone.

Under polarized light, Sharpey fibers (SF) are seen inserting into newly regenerated bone (NB) and cementum (NC). In the ground section, well-defined connective tissue fibers are also seen inserting into regenerated cementum. PDL = periodontal ligament.\textsuperscript{10}

*Results obtained in this trial are based on a technique that includes methods not included in approved insert. See Full Prescribing Information on page 14 & 15.
Baseline Miller Class II gingival recession defect

Following flap reflection and root preparation, rhPDGF-BB is placed onto the root surface.*

A porous collagen wound healing dressing placed over the graft site is partially saturated with blood and further hydrated with rhPDGF-BB* and secured with resorbable sutures at each papillary position.

GEM 21S® is placed onto the exposed root surface no closer than 3 mm above the CEJ

A full-thickness mucoperiosteal flap with divergent releasing incisions reveals 6 mm of labial bone loss

The mucoperiosteal flap is coronally repositioned to the level of the CEJ and secured with multiple interrupted sutures.

Six months post-op: the gingival margin remains at the level of the CEJ with no evidence of recession.

*This step in the procedure is not in the FDA approved labeling of the product.

*Results obtained in this trial are based on a technique that includes methods not included in approved insert. See Full Prescribing Information on page 14 & 15.
Patient presents with significant Miller Class 1 and 2 gingival recession defects on teeth numbers 5, 6 and 7. Note clefting on tooth number 7.

Following reflection of a full-thickness envelope flap, interdental papillae were de-epithelialized. Apical to the mucogingival juction, horizontal relaxing incisions in the periosteum were made to eliminate muscle tension and to facilitate tension-free coronal positioning of the mucosal flap.

Exposed portions of the roots were debrided and root-planed using curettes and finishing burs.

The exposed root surfaces were conditioned with EDTA for 2 minutes to remove the smear layer and then thoroughly rinsed with sterile saline.

HeliTape® was properly sized and shaped, wetted with sterile saline and sutured over the exposed root surfaces using 6-0 polygalactin sutures.

The sutured HeliTape® was folded incisally to allow proper placement of the GEM 21S® graft.

HeliTape® was carefully repositioned apically to cover the entire GEM 21S® graft.

The flap was coronally advanced without tension coronal to the level of the CEJ of each tooth and sutured interdentally with 6-0 polygalactin sutures.

GEM 21S® was carefully placed to cover all exposed root surfaces and adjacent bony areas. Sufficient volume of GEM 21S® was placed in order to create space for regeneration of the attachment apparatus to occur.

A 2-month post-operative visit demonstrates healthy gingival color and texture and maintenance of 100% root coverage.

Post-operative results at 9 months demonstrate stable gingival margins and the appearance of increased tissue thickness relative to baseline. Note the increase in keratinized tissue on teeth numbers 5 and 6.

Case by Dr. Jeffrey Ganeles
Long-Term Predictability

Patients from the GEM 21S® Growth-factor Enhanced Matrix pivotal trial continued to be monitored by their treating physicians for a total for 36 months. The data collected demonstrates the continued long-term efficacy of GEM 21S® treatment.

- The GEM 21S® group demonstrated significantly more bone fill over the β-TCP control throughout 36 months.
- It took more than 2 years for the β-TCP group to reach the level of bone fill achieved with GEM 21S® in only 6 months.

Radiographic Percent Bone Fill: 6 - 36 Months

Radiographic Linear Bone Growth: 6 - 36 Months

Clinical Attachment Level Gain: 6 - 36 Months
**Intrabony Defects: Long-Term Results**

Baseline measurement indicated a 10 mm probing depth for a defect at the distal aspect of tooth #19.

Baseline radiograph

Surgical exposure revealed an 8 mm deep x 4 mm wide 3-walled-circumferential intrabony defect.

Five year post-op radiograph indicates bone fill has been maintained to the level of the osseous crest with no evidence of ankylosis.

Baseline 13 mm probing depth on the distal aspect of tooth #19

Surgical exposure revealed a 7 mm deep x 4 mm wide circumferential 2-walled intrabony defect.

Five year post-op radiograph indicates the bony architecture and periodontal ligament space appear normal.

**Gingival Recession Defects: Long-Term Results**

Presurgical intraoperative measurements

Soft tissue root coverage six months following surgery

Soft tissue root coverage three years following surgery

Clinical evidence of approximately 2-3 mm bone growth over previously denuded root surface at three years

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Please see the complete article referenced at www.perio.org, or contact Osteohealth for a copy.
Clinical Instructions for Use

GEM 21S® Growth-factor Enhanced Matrix contains a recombinant human platelet derived growth factor (rhPDGF-BB) and a synthetic beta-tricalcium phosphate (β-TCP). Familiarization with this device and following proper surgical techniques are extremely important when using GEM 21S®.

All components are supplied sterile for single use only. The external surface of the rhPDGF-BB syringe and β-TCP cup are not sterile and therefore proper aseptic technique* should be followed when preparing GEM 21S® for use.

Remove a GEM 21S® kit from the refrigerator.

Remove tray from the carton. Inspect the components of the kit for structural integrity prior to use. If the seal of any inner or outer container is open, broken or otherwise damaged, the product must be assumed to be non-sterile and consequently must not be used.

Open peel-cup lid to β-TCP container and empty contents into a sterile bowl (e.g. dappen dish) on surgical tray.

Remove syringe of rhPDGF-BB from tray and fully saturate the sterile β-TCP particles with the rhPDGF-BB solution while in the sterile surgical field.

Allow the product to sit for approximately ten (10) minutes before implantation to allow the growth factor to bind to the β-TCP particles.

Following exposure of the defect, all granulation tissue must be carefully removed. Thorough soft tissue debridement of the defect site is critical to successful regeneration. Granulation tissue, if left in the defect, could be stimulated by the rhPDGF-BB component, diminishing the desired regenerative response. Exposed tooth root surfaces should also be thoroughly planed.

Using a sterile surgical instrument, completely fill the defect site to the level of the surrounding bony walls with the GEM 21S® graft. Overfilling should be avoided. Use moderate pressure, taking care not to crush the particles.

To enhance the formation of new bone, GEM 21S® should be placed in direct contact with well-vascularized bone. Excessive bleeding should be controlled prior to placing grafting materials. Primary closure should be obtained whenever possible. **Any remaining product must be discarded and not reused.** Pre-requisites for all regenerative procedures should include prevention of wound dehiscence, a stable clot, and minimal bacterial contamination.

*This information is supplementary to the GEM 21S® Full Prescribing Information provided on the next page.*
GEM 21S®
growth factor-enhanced matrix

Caution: Federal Law restricts this device to sale by or on the order of a dentist or physician.

DEVICE DESCRIPTION:
GEM 21S® is a completely synthetic grafting system for bone and periodontal regeneration composed of a purified recombinant growth factor and a synthetic calcium phosphate matrix. GEM 21S® is composed of two sterile components: synthetic beta-tricalcium phosphate (ß-TCP) (Ca₃(PO₄)₂) is a highly porous, resorbable osteoconductive scaffold or matrix that provides a framework for bone ingrowth, aids in preventing the collapse of the soft tissues and promotes stabilization of the blood clot. Porous diameters of the scaffold are specifically designed for bone ingrowth and range from 1 to 500 μm. The particle size ranges from 0.25 to 10.0 mm and highly purified, recombinant human platelet-derived growth factor-βB (rhPDGF-βB). PDGF is a native protein constituent of blood platelets. It is a tissue growth factor that is released at sites of injury during blood clotting. In vitro and animal trials have demonstrated GEM 21S®’s potent mitogenic (proliferative) angiogenic (neovascularization) and chondrogenic (directed cell migration) effects on bone and periodontal ligament derived cells. PDGF is known to be one protein involved in the multi-factorial and complex process of bone and wound repair. Animal studies have shown PDGF to promote the regeneration of periodontal tissues including bone, cementum, and periodontal ligament (PDL).

The contents of the cup of ß-TCP are supplied sterile by gamma irradiation. Sterile rhPDGF-βB is aseptically processed and filled into the syringes in which it is supplied.

INDICATIONS:
GEM 21S® is indicated to treat the following periodontally related defects:
• Intrabony periodontal defects;
• Periapical periodontal defects; and
• Gingival recession associated with periodontal defects.

CONTRAINDICATIONS:
As with any periodontal procedure where bone grafting material is used, GEM 21S® is CONTRAINDICATED in the presence of one or more of the following clinical situations:
• Untreated acute infections at the surgical site;
• Untreated malignant neoplasm(s) at the surgical site;
• Untreated acute infections at the surgical site; and
• Gingival recession associated with periodontal defects.

WARNINGS:
The exterior of the cup and syringe are NOT sterile. See directions for use. It is not known if GEM 21S® interacts with other medications. The use of GEM 21S® with other drugs has not been studied. Camouflage and reproductive toxicity studies have not been conducted. The safety and effectiveness of GEM 21S® has not been established:
• In non-periodontal bony locations, including other tissues of the oral and craniofacial region such as bone graft sites, tooth extraction sites, bone cavitons after cystectomy, and bone defects resulting from traumatic or pathologic origin. GEM 21S® has also not been studied in situations where it would be augmenting autogenous bone and other bone grafting materials;
• In pregnant and nursing women. It is not known whether rhPDGF-βB is excreted in the milk of nursing women;
• In pediatric patients below the age of 18 years;
• In patients with teeth exhibiting mobility of greater than Grade II or a Class III function;
• In patients with frequent or excessive use of tobacco products.

Consideration should be given to alternative therapies prior to performing bone grafting in patients:
• Who have severe endocrine-induced bone diseases (e.g. hyperparathyroidism);
• Who are receiving immunosuppressive therapy; or
• Who have known conditions that may lead to bleeding complications (e.g. hemophilia).

The GEM 21S® grafting material is intended to be placed into periodontally related defects. It must not be injected systemically. The radioactivity of GEM 21S® is comparable to that of bone and diminishes as GEM 21S® is resorbed. The radioactivity of GEM 21S® must be considered when evaluating radiographs as it may mask underlying pathological conditions.

PRECAUTIONS:
GEM 21S® is intended for use by clinicians familiar with periodontal surgical grafting techniques. GEM 21S® is supplied in a single use kit. Any unopened unused material must be discarded and components of this system should not be used separately.

HOW GEM 21S® IS SUPPLIED:
Each GEM 21S® kit consists of:
• (1) one cup containing 0.5 cc of ß-TCP particles (0.25 to 1.0 mm); and
• (2) one syringe containing a solution of 0.5 ml rhPDGF-βB (0.3 mg/ml).

All of these components are for single use only.

CLINICAL STUDY:
A 180 patient, double-blinded, controlled, prospective, randomized, parallel designed multicenter clinical trial in subjects who required surgical intervention to treat intrabone periodontal defects was completed. The major inclusion criteria were:
• No localized aggressive periodontal disease
• Treatment site with the following characteristics:
  • Probing pocket depth ≥ 7mm at baseline;
  • After surgical debridement, ≥2 mm vertical bone defect with at least 1 mm bony wall;
  • Sufficient keratinized tissue to allow complete tissue coverage of defect, and
  • Radiographic base of defect ≥3 mm coronal to the apex of the tooth.

The major exclusion criteria were:
• No periodontal surgery on the subject tooth within the last year;
• No significant recent tobacco use.
• Allergy to yeast-derived products;
• Using an investigational therapy within the past 30 days.

The duration of the study was six (6) months following implantation of the product. Patients were randomized into three patient treatment groups:
• Group I (n=60): ß-TCP and 3.0 mg/ml rhPDGF-βB (GEM 21S®)
• Group II (n=61): ß-TCP and 1.0 mg/ml rhPDGF-βB
• Group III (n=60): ß-TCP and buffer alone (active control)

The baseline characteristics among the subjects in each group were similar with the exception of “base of defect to root apex.” Group I had a mean defect which was significantly less than Group II (6.5 mm vs. 7.7 mm, p<0.04).

Schedule of Patient Visits
Patients had 4 visits over the 6 months prior to surgery and device implantation. Scaling and root planing were performed if necessary within 3 months prior to the implant surgery date (Visit 5). Following implantation, subjects underwent 4 follow-up visits during the first 24 days to assess wound healing and pain assessment and then 4 further follow-up visits every 6 weeks through 6 months. At these latter visits, clinical measurements and radiographs were performed.

Endpoints
The pre-defined primary effectiveness endpoint was the mean change in CAL between baseline and 6 months. Results were to be compared 1) for each group to a historically established level of effectiveness (mean change of 1.5 mm) and 2) between Group I and Group III. The pre-defined secondary endpoints included:
• Comparison of linear bone growth (LBG);
• Comparison of % bone defect fill (BDF) based on radiographs
• Area under the curve for change in CAL
• Change in CAL between baseline and 6 months
• Pocket depth reduction (PDR) change between baseline and 6 months
• Gingival recession (GR) change between baseline and 6 months
• Wound healing during first 3 weeks post-operatively

Primary Endpoint Results
The primary effectiveness endpoint was evaluated using the mean change in CAL gain (mm) from baseline to 6 months for each of the three groups. Mean changes at 6 months are presented in the Table below.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group and Change</th>
<th>Control Group and Change</th>
<th>Difference in Means</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>3.7 mm</td>
<td>1.5 mm</td>
<td>2.2 mm</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group II</td>
<td>3.7 mm</td>
<td>1.5 mm</td>
<td>2.2 mm</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group III</td>
<td>3.5 mm</td>
<td>1.5 mm</td>
<td>2.0 mm</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

As seen in the table above, all three groups, including the control group, had statistically and clinically meaningful mean CAL gains when compared to the historically established 1.5 mm level (p<0.001). At 6 months, there was no statistically or clinically significant difference in CAL gain for the low-concentration group (Group I) when compared to the active control without GEM 21S® (p=0.20). However, at 3 months (not included in the Table above), the difference was 0.5 mm (3.8 mm vs 3.3 mm) which was statistically significant (p=0.04) suggesting that the device may facilitate earlier resolution of periodontal intrabony lesions.

Secondary Endpoint Results
As noted above, numerous secondary endpoints were pre-defined in the clinical protocol. The results for these are presented in the Table below. The results represent changes from baseline to 6 months unless otherwise noted.

Parameter | Primary Group and Mean Change | Control Group and Mean Change | Difference in Means | p-value |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear Bone Growth</td>
<td>Group I 2.52 mm</td>
<td>Group III 0.89 mm</td>
<td>1.63 mm</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Group II 1.53 mm</td>
<td>Group III 0.89 mm</td>
<td>0.64 mm</td>
<td>0.02</td>
</tr>
<tr>
<td>% Bone Fill</td>
<td>Group I 56.0%</td>
<td>Group III 17.9%</td>
<td>38.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Group II 33.9%</td>
<td>Group III 17.9%</td>
<td>16.0%</td>
<td>0.02</td>
</tr>
<tr>
<td>AUC for CAL Gain (mm-weeks)</td>
<td>Group I 87.5</td>
<td>Group III 60.1</td>
<td>27.4</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Group II 81.8</td>
<td>Group III 60.1</td>
<td>21.7</td>
<td>0.35</td>
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<tr>
<td>CAL Gain</td>
<td>Group I 3.7 mm</td>
<td>Group III 3.5 mm</td>
<td>0.2 mm</td>
<td>0.29</td>
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<tr>
<td></td>
<td>Group II 4.4 mm</td>
<td>Group III 4.2 mm</td>
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<td>0.38</td>
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<tr>
<td></td>
<td>Group III 4.3 mm</td>
<td>Group II 4.2 mm</td>
<td>0.1 mm</td>
<td>0.66</td>
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<tr>
<td>PDR - 3 Months*</td>
<td>Group I 4.2 mm</td>
<td>Group II 4.2 mm</td>
<td>0.0 mm</td>
<td>0.80</td>
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<tr>
<td></td>
<td>Group II 4.1 mm</td>
<td>Group III 4.2 mm</td>
<td>0.1 mm</td>
<td>0.67</td>
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<tr>
<td>GR</td>
<td>Group I 0.7 mm</td>
<td>Group III 0.7 mm</td>
<td>0.0 mm</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>Group II 0.6 mm</td>
<td>Group III 0.7 mm</td>
<td>0.1 mm</td>
<td>0.81</td>
</tr>
<tr>
<td>GR - 3 Months*</td>
<td>Group I 0.5 mm</td>
<td>Group III 0.9 mm</td>
<td>0.4 mm</td>
<td>0.04</td>
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<tr>
<td></td>
<td>Group II 0.7 mm</td>
<td>Group III 0.9 mm</td>
<td>0.2 mm</td>
<td>0.46</td>
</tr>
</tbody>
</table>

* Not a pre-defined secondary or primary endpoint.

The table illustrates that both the low- and high-dose device achieved significant improvement over the control device (rhPDGF-βB) at 6 months for linear bone growth and percent bone fill. Although other parameters (CAL gain and gingival recession) showed significant changes at 3 months for the high-dose group, these benefits were not maintained over control at 6 months. Again, several of these results suggest that the device facilitates earlier resolution of periodontal intrabony lesions.
Long-Term follow-up
Throughout the 24-month observation period, study data demonstrated the continued long-term efficacy of GEM 21S® treatment. Radiographic (x-ray) analysis of bone growth showed that over the 24-month observation period, all treatment groups demonstrated an increase in bone fill. At the end of the 24-month observation period, the GEM 21S® group demonstrated a statistically significant greater amount of bone formation compared to the ß-TCP matrix alone. In addition, after 24 months, the ß-TCP group failed to experience the level of radiographic bone fill that was achieved by the GEM 21S® group at the end of the first six months of the trial.

Comparison of Emdogain® and GEM 21S® Pivotal Clinical Trial Results
The table below compares the results obtained in the GEM 21S® pivotal clinical trial to two safety and efficacy studies submitted as part of the Emdogain® PMA application. Improvements in clinical and radiographic parameters in the GEM 21S® trial compare favorably with, or exceed, documented outcomes for other regenerative therapies in studies examining defects with similar baseline characteristics.

DIRECTIONS FOR USE:
ASEPTIC TECHNIQUE:
- The contents of the cup of ß-TCP are sterilized by gamma radiation.
- Sterile mPDGF-BB is aseptically processed and filled into the syringe in which it is supplied.

INNOVATIVE DENTAL SOLUTIONS
Division of Luitpold Pharmaceuticals, Inc.
One Luitpold Drive
PO Box 9001
Shirley, NY 11967 USA
(800) 874-2334

Sterile Cup Made in Gt. Britain
This product is sold and distributed under US patents:
4,845,075
5,045,633
5,124,316
7,473,678

IN0005 November 2011
References

4. www.harvesttech.com/biomaterials/references.htm
8. PMA #040013: Data on file, Luitpold Pharmaceuticals, Inc.

IMPORTANT SAFETY INFORMATION

GEM 21S® Growth-factor Enhanced Matrix is intended for use by clinicians familiar with periodontal surgical grafting techniques. It should not be used in the presence of untreated acute infections or malignant neoplasm(s) at the surgical site, where intra-operative soft tissue coverage is not possible, where bone grafting is not advisable or in patients with a known hypersensitivity to one of its components. It must not be injected systemically.

The safety and effectiveness of GEM 21S® has not been established in other non-periodontal bony locations, in patients less than 18 years old, in pregnant or nursing women, in patients with frequent/excessive tobacco use (e.g. smoking more than one pack per day) and in patients with Class III furcations or with teeth exhibiting mobility greater than Grade II. In a 180 patient clinical trial, there were no serious adverse events related to GEM 21S®; adverse events that occurred were considered normal sequelae following any periodontal surgical procedure (swelling, pain).

Osteohealth is a leading provider of high-quality, first-in-class, innovative products for the dental industry. Since 1994, Osteohealth has been dedicated to developing and marketing products that are scientifically and clinically proven to enhance patient care. Products including GEM 21S® Growth-factor Enhanced Matrix, Mucograft® collagen matrix, and now Equimatrix® natural bone mineral matrix are technologies that represent our commitment to providing unique, innovative solutions to unmet clinical needs.

Osteohealth is a division of Luitpold Pharmaceuticals, Inc., a wholly owned subsidiary of Daiichi Sankyo Co., Ltd, a multinational corporation and one of Japan’s leading pharmaceutical companies.

Incorporate GEM 21S® into your practice today by calling our Customer Service Representatives at 1-800-874-2334

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