SYNOPSIS OF THE CLINICAL STUDY REPORT

Name of Sponsor	Genera Research Ltd.
Name of Finished Product	Osteogrow, powder and solvent for implantation paste
Name of Active Ingredient	Recombinant human bone morphogenetic protein 6 (rhBMP6)

Title of Study: Safety, tolerability, rhBMP6 pharmacokinetics and efficacy of a single dose of Osteogrow (rhBMP6 in autologous Whole Blood Coagulum Derived [WBCD] carrier) delivered locally to the fracture site in adult patients with a closed distal radius fracture.

Protocol number: GR-OG-279239-01; **EudraCT number**: 2014-005101-21

Study Centers and Countries: Two centers, located in Croatia, and Bosnia and Herzegovina.

Publication: Preliminary results of the trial were published in: Durdevic D, Vlahovic T, Pehar S, et al. A novel autologous bone graft substitute comprised of rhBMP6 blood coagulum as carrier tested in a randomized and controlled Phase I trial in patients with distal radial fractures. Bone. 2020;140:115551. doi: 10.1016/j.bone.2020.115551.

Study Period: 27-DEC-2015 (first-patient-first-visit) to 02-SEP-2019 (last-patient-last-visit).

Phase of Development: I/II

Background and Rationale for the Study: Bone morphogenetic proteins (BMPs) are known natural inducers of bone formation. Two BMPs, rhBMP2 and rhBMP7, have been approved for therapeutic use in humans. These rhBMPs are locally administered using bovine collagen as a carrier, a xenogeneic protein with consequent risks of proinflammatory effects and untoward immune responses. Genera is developing a novel BMP-based drug called Osteogrow, or autologous bone graft substitute (ABGS). Osteogrow contains rhBMP6, a paralogue of rhBMP7, delivered in autologous WBCD carrier, which is essentially a patient's blood clot.

Present study is the first-in-human (FiH) trial of rhBMP6/Osteogrow, intended to obtain first data on the safety, tolerability and pharmacokinetics (PK) of rhBMP6 upon local dosing in the WBCD carrier. As BMPs inevitably trigger bone formation, the study had to be conducted in subjects who potentially may benefit from such action, allowing for initial assessment of efficacy as well.

Distal radius fracture (DRF) was selected as the target indication because it is one of the most common fracture types. Closed DRFs generally heal well, yet, around three months are needed for recovery. The ability to accelerate bone healing in patients with DRF is expected to result in a faster regain of arm function, reducing the disability and absenteeism associated with DRF.

Objectives: Primary objectives were (a) to evaluate the safety and tolerability of a single dose of Osteogrow delivered locally to the closed DRF site; and (b) to evaluate systemic PK of rhBMP6 after single dose of Osteogrow delivered locally to the DRF site.

Secondary objectives were (a) to explore the relationship between systemic PK and systemic safety/ tolerability; and (b) to explore the efficacy of Osteogrow in patients with a closed DRF.

Methodology: The study was designed as a randomized, placebo-controlled, double-blind, single dose, parallel group, multicenter trial, with a randomized, evaluator-blinded, second control arm

receiving the standard of care (SoC) only. SoC consisted of fracture reduction with radiologic check-up, fixation with Kirschner wires (K-wires) and temporary immobilization by splint or external fixator over 5 weeks, followed by routine physical therapy for approximately 21 days.

Eligible patients were randomized to one of the following groups in a 1:1:1 ratio overall:

- **SoC** (no-treatment control in terms of local medical therapy);
- **Placebo** (PBO): SoC + rhBMP6 excipients in WBCD, 1.0 mL, injected into the fracture gap after fracture fixation;
- **Osteogrow**: SoC + 250 μg rhBMP6 in WBCD, 1.0 mL, injected into the fracture gap after fracture fixation.

Osteogrow and PBO were administered and evaluated in a double-blind manner; the absence of drug administration in the SoC group could not be masked, but all radiological assessments and hand function measurements were performed in a blinded manner. To ensure the safety of study participants, patients were to be enrolled in several stages, which were divided by a 7-day follow-up of the last patient included in the preceding stage, and safety data review by the Independent Drug Safety Monitoring Board (IDSMB). These stages were defined as follows:

- **Stage 1A** (FiH part): 19 patients randomized in a 5:7:7 ratio to SoC, PBO and Osteogrow across the three clusters of three patients each (randomized in a 1:1:1 ratio), followed by two clusters of five patients each (randomized in a 1:2:2 ratio). Within each cluster, enrolment of the next patient was staggered by at least 48 hours, if the preceding patient had received blinded local treatment (Osteogrow or PBO). Between clusters, excluding the last one, enrolment was staggered by at least 7-day follow-up of the last preceding patient who received blinded treatment. The first three clusters were to be enrolled at one study site, and the last two could have been enrolled in parallel at up to two sites. All patients were to be hospitalized for 72 hours after surgery.
- **Stage 1B**: 17 patients randomized in a 7:5:5 ratio to SoC, PBO and Osteogrow. At the study site, enrolment was to be staggered by at least 48 hours, if the preceding patient had received blinded treatment. Patients were to be hospitalized for 48 hours after surgery.
- **Stage 2**: 39 patients randomized in a 1:1:1 ratio to SoC, PBO and Osteogrow, with same enrolment restrictions and hospitalization requirements as in Stage 1B.

Across the stages, patients were screened within three days before the day of surgery/study treatment (study Day 1). Post-treatment assessments were performed during hospital stay (on Days 1, 2 and 3), at follow-up visits scheduled 1, 2, 3, 5, 7, 9, 11 and 13 weeks after surgery, and at Week 26 (post-study follow-up). Visits on Weeks 1, 2 and 3 were due for Stage 1A/B patients only. Follow-up included clinical, laboratory and radiological procedures/tests, in accordance with the criteria for evaluation, information on concomitant medication, and regular pregnancy tests in women of child-bearing potential. Blood and urine sampling for PK assays, and blood sampling for anti-rhBMP6 antibody test were limited to patients who received blinded local treatment, with the exception of baseline samples which were collected from all patients.

All X-rays (anteroposterior and lateral) and computed tomography (CT) scans obtained before surgery and at Weeks 5, 9, 13 and 26 were pseudonymized and reviewed by three evaluators in a blinded manner. Based on X-ray and CT findings, each evaluator rated each of the four indicators of fracture healing (formation of callus, trabecular fracture line closure, rebridgement of cortices and trabecular resorption area) at Weeks 5, 9 and 13 using a 3-grade scale ranging from 0 to 2, where higher scores indicated better healing. They also assessed the completeness of cortical rebridgement at Weeks 13 and 26, the completeness of trabecular bone reconstruction at Week 26, and the presence of soft tissue ossification/calcifications at all time points.

Number of Patients

Planned: 75 (25 per treatment group).

Actual: 32 (Osteogrow 10, PBO 11, and SoC 11).

The study was prematurely terminated after inclusion of 32 patients due to slow enrolment.

Diagnosis and Main Criteria for Inclusion and Exclusion

Diagnosis: Closed DRF.

Main inclusion criteria: Adult males and females (≥18 years) with unilateral, dorsally angulated closed DRF sustained within previous 72 hours and needing reduction and stabilization by K-wires, but no open surgery; otherwise healthy (no clinically relevant abnormalities detected at screening) and willing to take part in the study and comply with study requirements.

Main exclusion criteria: Pregnancy, breastfeeding a child, or planning to become pregnant within the next 6 months; previous fracture or bone surgery in the currently fractured distal forearm; joint diseases affecting the function of the wrist and/or hand of the injured arm; history of diabetes mellitus, or history of symptomatic nephro- or urolithiasis within two years; previous treatment with rhBMPs, or use of corticosteroids within 7 days prior to surgery.

Test Product, Dose, Mode of Administration, Batch Number(s)

Test product: rhBMP6 delivered in autologous WBCD carrier (Osteogrow). rhBMP6 was supplied in the form of rhBMP6 0.5 mg vials and as part of Osteogrow kit composed of Box A (containing one rhBMP6 0.5 mg vial) and Box B (containing one 10 mL ampoule of water for injection, one 5 mL ampoule of Calcium Chloride Injection 5 mmol/5 mL, and ancillary items needed for implant preparation like syringes, needles and similar). Osteogrow was prepared within 60 to 90 minutes before administration using Osteogrow kit and 1 mL of the patient's peripheral blood.

Dose: 250 µg rhBMP6 in 1 mL WBCD carrier.

Mode of administration: Transcutaneous injection into the fracture gap via a dorsal approach and under fluoroscopic control, after fracture reduction and fixation with K-wires and, if applicable, external fixator.

Duration of Treatment: Single administration.

Control Product and Other Reference Treatments

- **PBO group**

  Control product: rhBMP6 excipients delivered in autologous WBCD carrier (PBO). rhBMP6 excipients were supplied in the form of rhBMP6 Placebo vials, were visually identical to rhBMP6 0.5 mg vials, and provided as part of Osteogrow kit (Box A). PBO was prepared in the same manner as Osteogrow, yielding a coagulum visually identical to Osteogrow.

  Dose: 1 mL WBCD carrier.

  Mode of administration: In the same manner as the test product.

- **SoC group:** Fracture reduction with radiologic check-up, fixation with K-wires and temporary immobilization by splint or external fixator over 5 weeks, followed by routine physical therapy for a total of approximately 21 days.

Criteria for Evaluation (Endpoints)

Primary safety and tolerability endpoints:

- The incidence and type of treatment-emergent adverse events (TEAEs) in the Osteogrow group

compared to the PBO and the SoC group.

- The incidence of soft tissue ossification/calcifications at the DRF site in the Osteogrow group compared to the PBO and the SoC group, based on clinical examination (palpation of the fracture site) at 1, 2 and 3 weeks, and radiology findings at 5, 9, 13 and 26 weeks after surgery.
- The incidence and severity of clinical signs of inflammation at the DRF site (edema, erythema, tenderness and pain) in the Osteogrow group compared to the PBO and the SoC group, based on the investigator's assessment on study days 2 and 3, and at 1, 2, 3, 5, 7, 9, 11 and 13 weeks after surgery.
- Pain intensity in the Osteogrow group compared to the PBO and SoC group, based on the patient's assessment of pain using a numeric rating scale (NRS) at 6 and 12 hours after surgery, on study days 2 and 3, and at 1, 2, 3, 5, 7, 9, 11 and 13 weeks after surgery.

Other safety endpoints:

- The occurrence of anti-rhBMP6 antibodies at 13 and 26 weeks after surgery.
- Treatment effects on safety laboratory parameters (hematology, clinical chemistry and urinalysis) on study days 2 and 3, and at 1, 2, 3, 5, 7, 9, 11 and 13 weeks after surgery.
- Treatment effects on vital signs, including blood pressure (BP) and heart rate (HR) at 0.25, 1 and 2 hours after Osteogrow/PBO dosing (or placement of the third K-wire in the SoC group), and BP, HR, respiratory rate and body temperature on study day 2, and at 1, 2, 3, 5, 7, 9, 11 and 13 weeks after surgery.
- Treatment effects on physical examination findings on study day 2 and at 1, 2, 3, 5, 7, 9, 11 and 13 weeks after surgery.
- Treatment effects on ECG findings at 1, 6, 24 and 48 hours after Osteogrow/PBO dosing (or the placement of the third K-wire in the SoC group), and 13 weeks after surgery.
- Treatment effects on hand function, evaluated by the patients using the Disabilities of the arm, shoulder and hand (DASH) questionnaire at 5, 7, 9, 11 and 13 weeks after surgery.
- Treatment effects on wrist range of motion (ROM) and grip strength at 7, 9, 11 and 13 weeks after surgery.

PK endpoints:

- rhBMP6 concentration in plasma at screening and on Day 1, before surgery (pre-dose) and at 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 12 and 24 hours after Osteogrow or PBO administration.
- rhBMP6 concentration in urine at screening, and in a 0-24 hours urine collection after Osteogrow or PBO administration.
- PK parameters for rhBMP6, derived from plasma and urine concentrations, including: time to peak concentration in plasma (Tmax), peak concentration in plasma (Cmax), area under the plasma concentration-time curve (AUC) from time zero until 24 hours post-dose (AUC0-24), AUC extrapolated to infinity (AUC0-inf), mean residence time in plasma (MRT), apparent total body clearance after orthotopic administration ($CL_{T/F}$), apparent volume of distribution (Vd), elimination rate-constant (λz), elimination half-life (t1/2), renal clearance (CL_R), and non-renal clearance (CL_{NR}).

Efficacy endpoints:

- The incidence of early healing success in the Osteogrow group compared to the PBO and the SoC group, defined as a cumulative score for callus formation ≥5 at 5 weeks after surgery.
- The incidence of late healing success in the Osteogrow group compared to the PBO and the SoC

group, defined as a cumulative score for cortical rebridgement ≥5 at 9 weeks after surgery.

- Time-averaged proportion of bone healing successes (clearly visible callus at Week 5 and cortical bridging in at least 3 out of 4 cortices at Week 9) in the Osteogrow group compared to the PBO and the SoC group combined, if data allow.
- Mean total score over time for each of the four indicators of bone healing (callus formation, trabecular fracture line closure, cortical rebridgement and trabecular resorption area) in the Osteogrow group compared to the PBO and the SoC group, where total score over time is defined as the sum of scores at 5, 9 and 13 weeks after surgery.
- Mean total radiology score at 5, 9 and 13 weeks after surgery in the Osteogrow group compared to the PBO and the SoC group, where total radiology score is defined as the sum of scores for the four indicators of bone healing (callus formation, trabecular fracture line closure, cortical rebridgement and trabecular resorption area).
- The incidence of complete cortical rebridgement (all four cortices rebridged) at 13 and 26 weeks after surgery in the Osteogrow group compared to the PBO and the SoC group.
- The incidence of complete reconstruction of trabecular bone at 26 weeks after surgery.

Statistical Methods

General approaches: Data sets for safety, PK and efficacy (intention-to-treat) analyses comprised all randomized patients who underwent surgery. All relevant data were individually listed and summarized by treatment group. For between-group comparisons, data distribution was first assessed using the Kolmogorov-Smirnov test and, depending on the obtained p-value, either a parametric (if $p \geq 0.05$) or non-parametric (if $p < 0.05$) version of the planned test was applied. All p-values <0.05 were considered significant.

Safety and tolerability analyses: All adverse events (AEs) were coded using MedDRA, version 19.0 or later, and tabulated by treatment group and system organ class/preferred term. The incidence of AEs, TEAEs and key subcategories of AEs/TEAEs was compared between groups by the Fischer-Freeman-Halton (FFH) test, which was also used to compare the incidence of soft tissue ossification/calcifications at each time point. Scores for clinical signs of inflammation at the fracture site, pain NRS scores, wrist ROM, grip strength and DASH scores were analyzed by the Friedman test to detect changes over time and by the Kruskal-Wallis test to detect differences between groups at each time point. Other safety endpoints were analyzed only descriptively.

PK analyses: Available PK data were summarized by treatment group.

Efficacy analyses: Radiological scores (cumulative score for each parameter at each time point, total score over time for each parameter, and total radiology score at each time point) were calculated from raw data. The incidence of early and late healing success was compared between groups by the FFH test if data allowed. Time-averaged proportion of bone healing successes was to be analyzed by fitting a generalized linear mixed model (treatment [dichotomized as "Osteogrow" and "control"], time, time*treatment interaction, age and sex) to proportion of successes at Weeks 5 and 9; however, available data allowed for the modelling of the late healing success only. All radiological scores were analyzed by the repeated measures analysis of variance (rm ANOVA) with Bonferroni correction where applicable. Also, the effect sizes (Cohen's *d* values) were calculated for pairs of trial arms for each score and time point; the effect size *d* of 0.2 to <0.5 was considered low, 0.5 to <0.8 medium, and ≥0.8 high. The incidence of complete cortical rebridgement at Weeks 13 and 26, and the incidence of complete reconstruction of

trabecular bone at Week 26 was compared between groups by the FFH test. *Post-hoc*, the total radiology score at all time points was calculated for each group and compared between groups using one-way ANOVA; also, total radiology scores at Weeks 5 and 9 only were compared between groups by the rm ANOVA with Bonferroni correction.

Sample size: The trial was prematurely terminated resulting in sample size of 10 to 11 patients per group. Given the purpose and objectives of the trial, this sample size is still considered sufficient to describe the PK characteristics of rhBMP6 after local administration in WBCD carrier, and to obtain a rough estimate of Osteogrow safety, tolerability and pharmacodynamic effect on DRF healing, based on numerical trends across study groups and exploratory comparisons.

Summary of Results

Patient disposition: Thirty-two patients were screened and enrolled in the trial: 10, 11 and 11 in the Osteogrow, PBO and SoC groups, respectively. All received a randomly allocated treatment and 10 (100%), 8 (73%) and 10 (91%), respectively, completed the trial. This includes one patient from the SoC group who completed the trial before the Week 26 visit became mandatory for all patients. Two patients from the PBO group withdrew consent and left the trial after 3 weeks or 13 weeks of follow-up, and two were lost to follow-up: one (SoC) after 7 weeks and the other (PBO) after 9 weeks. All 32 patients were included in all analyses.

Demography and baseline characteristics: Study population consisted of 28 women and four men at the age of 21 to 75 years. Treatment groups were comparable in terms of age (mean age per group ranged from 50.6 to 60.6 years; p=0.305, one-way ANOVA), sex (82% to 100% of patients were female; p=0.512, FFH test), body mass index (means per group were 25.3 to 27.3 kg/m^2; p=0.422, one-way ANOVA), renal function (means per group for creatinine clearance were 87.6 to 104.2 mL/min; p=0.387, one-way ANOVA), smoking (0% to 27% of patients were smokers; p=0.427, FFH test), and fracture duration before study treatment (means per group were 1.3 to 1.7 days; p=0.160, one-way ANOVA). The most common comorbidity was hypertension, which was present in 3 (30%), 1 (9%) and 2 (18%) patients in the Osteogrow, PBO and SoC groups, respectively. One patient in each of the PBO and SoC groups had a concurrent fracture of the ipsilateral ulna.

Safety and tolerability results: A total of 72 AEs in 25 (78.1%) patients overall were reported during the trial. Of these, 65 events were TEAEs: 20 in 7 (70%) patients in the Osteogrow group, 21 in 8 (72.7%) patients in the PBO group and 24 in 9 (81.8%) patients in the SoC group. The number of patients with any AE or TEAE was similar between groups (p =0.757 and p=0.884; FFH test). The most common TEAEs were hypertension (21 episodes in 10 patients), tachycardia (15 episodes in 10 patients), and pyrexia (five episodes in four patients). Three SAEs were reported in total, in 1 (10%) patient in the Osteogrow group (upper limb fracture) and 2 (18.2%) patients in the SoC group (myocardial infarction and urinary tract infection); p=0.512, FFH test.

All SAEs resolved and no patient died during the study. Most events were mild and only three were severe (all SAEs). No AE/TEAE led to withdrawal from the study, nor was considered by the investigator to be related to study treatment.

There were no relevant differences between groups in hematology, blood chemistry and urinalysis findings, vital signs, general physical examination findings and ECG findings.

Soft tissue ossification was observed in one patient in the Osteogrow group in Week 9. It occurred on the dorsal side of the radius, was asymptomatic and partially resorbed by Week 26. Pain scores, wrist ROM, grip strength and DASH scores of this patient were similar to those reported in other patients.

Clinical signs of inflammation (edema, erythema, tenderness and pain) were mild to moderate in all groups and in most patients resolved within a week after surgery. Changes over time were statistically significant for all signs in all groups (p-values ranged from <0.001 to 0.029; Friedman test) with no differences between groups at any time point (p>0.05 for all comparisons; Kruskal-Wallis test).

Patient-reported pain scores also decreased over time in all groups. Changes in NRS scores were statistically significant in the Osteogrow and PBO groups, but not in the SoC group (p=0.034, p=0.008 and p=0.132, respectively; Friedman test), likely due to the small number of complete observations. Pain NRS scores were similar between groups except at 12 h and 48 h after surgery when these were lower in the Osteogrow group relative to SoC (p=0.025 at 12 h) or PBO (p=0.029 at 48 h); Kruskal-Wallis test with Bonferroni correction.

Wrist ROM was reduced at Week 7 in all groups. By Week 13, mean ROM values for radial and ulnar deviation were normal in all groups, pronation almost reached normal, while palmar flexion, dorsal flexion, and supination were improved but partially recovered. Significant changes over time were confirmed by the Friedman test for all movements in all groups (p-values ranged from <0.001 to 0.028), except for ulnar deviation in the PBO group (p=0.577), for pronation in the PBO and SoC groups (p=0.581 and p=0.069, respectively), and for radial deviation in all groups (p>0.05 in all groups). This likely occurred due to the small window for improvement in these movements coupled with the small sample size. Grip strength also significantly improved in all groups (p-values ranged from <0.001 to 0.003; Friedman test), but partially recovered by Week 13. There were no significant differences between groups in any wrist movement or grip strength at any time point (p>0.05 for all comparisons; Kruskal-Wallis test).

DASH disability and DASH work scores also improved in all groups. Significant changes over time were confirmed by the Friedman test for DASH disability scores in all groups (p-values ranged from <0.001 to 0.011), and for DASH work scores in the Osteogrow group only (p=0.010), probably due to the small number of complete observations in the other two groups. Only five patients completed the sports module of the DASH questionnaire. DASH sports scores improved in all of them. There were no significant between-group differences in any DASH score at any time point (p>0.05 for all comparisons; Kruskal-Wallis test).

Anti-rhBMP6 antibodies were not detected in any patient.

PK results: rhBMP6 was not detected in any plasma sample, so PK parameters could not be calculated.

Efficacy results: Cumulative scores for each of the four indicators of bone healing increased over time (p<0.001 for all scores, rm ANOVA with Bonferroni correction). Scores for cortical rebridgement were higher in the Osteogrow group compared to both the PBO and SoC groups (p=0.027 and p=0.010, respectively, rm ANOVA with Bonferroni correction). Other cumulative scores were similar between groups (p=0532 for callus formation, p=0.498 for trabecular fracture line closure, and p=0.848 for trabecular resorption area; rm ANOVA).

Cumulative scores for callus formation were low in all groups at all time points and no patient met the criteria for early healing success. Late healing success occurred in 10/10 (100%), 6/10 (60%) and 7/10 (70%) evaluable patients in the Osteogrow, PBO and SoC groups, respectively (p=0.151, FFH test). Neither the treatment arm (dichotomized into Osteogrow and “control”), age, nor sex, were predictors of late healing success (p=0.999, p=1.000 and p=1.000, respectively; GLMM).

The total score over time for cortical rebridgement was significantly higher in the Osteogrow group compared to PBO (p=0.005; rm ANOVA with Bonferroni correction). The difference vs. SoC did not reach statistical significance (p=0.069), but the effect size was large (Cohen’s *d* 1.72)

and the 95% confidence interval for the difference was skewed to the right (-0.051 to 1.785). Total scores over time for other indicators of bone healing were similar between groups.

Mean total radiology scores were similar in all groups at Week 13 (6.53 [SD 0.706], 6.50 [0.471] and 6.47 [0.757] in the Osteogrow, PBO and SoC groups, respectively), but were numerically higher in the Osteogrow group at Week 5 (3.87 [0.945] vs. 2.90 [1.112] and 2.90 [1.123]) and Week 9 (5.87 [0.632] vs. 5.13 [0.820] and 5.13 [0.919], respectively). No significant between-group differences were found at any time point by one-way ANOVA, however, *post-hoc* comparison of scores at Weeks 5 and 9 by using the rm ANOVA and Bonferroni correction showed significant differences between Osteogrow and both PBO (p=0.027) and SoC (p=0.027).

Cortical rebridgement was complete by Week 13 in all patients in the Osteogrow group and ~90% of patients in the PBO and SoC groups (p=0735, FHH test). By Week 26, it was complete in all evaluable patients and the trabecular bone was completely reconstructed in 4/7 (57.1%), 4/6 (66.7%) and 7/8 (87.5%) patients, respectively (p=0.491, FFH test).

Conclusions:

- Osteogrow was well-tolerated and safe after intraosseous administration in the fracture gap of the distal radius. TEAEs were common, but were mostly mild, equally frequent after treatment with Osteogrow, PBO or SoC, and generally similar between groups (mainly hypertension, tachycardia, and pyrexia). One event in the Osteogrow group (upper limb fracture) and two in the SoC group (myocardial infarction and urinary tract infection) were serious. These were the only severe TEAEs and resolved during the trial. No TEAE was related to study treatment in the investigator's opinion.
- The tolerability and safety of Osteogrow are further supported by the absence of relevant differences between groups in clinical laboratory findings (hematology, blood chemistry and urinalysis), vital signs, physical examination and ECG findings, clinical signs of inflammation, and functional outcomes (wrist ROM, grip strength and DASH scores). Moreover, patients treated with Osteogrow reported less pain at 12 h and 48 h after surgery compared to those treated with SoC or PBO, respectively.
- Asymptomatic soft tissue ossification on the dorsal side of the distal radius was observed in one patient treated with Osteogrow. It partially resorbed during follow-up and is expected to disappear over time as it has no function.
- No patient treated with Osteogrow developed anti-rhBMP6 antibodies.
- No rhBMP6 was detected in plasma after intraosseous administration of Osteogrow indicating negligible systemic exposure when delivered in the WBCD carrier.
- Osteogrow accelerated DRF healing as evident from significantly higher cumulative scores for cortical rebridgement in the Osteogrow group compared to PBO and SoC, a higher "total score over time" for cortical rebridgement compared to PBO (difference vs. SoC did not reach statistical significance likely due to small sample size), and higher total radiology scores at Weeks 5 and 9 compared to both PBO and SoC. While there were no statistically significant differences between groups in fracture healing success rates at Weeks 5 and 9, the latter was numerically higher in the Osteogrow group (100% vs. 60% and 70% in the PBO and SoC groups, respectively).

Date of Report: 26-MAR-2024