Genoterosil

Gene therapy for accelerating bone regeneration

Project Overview

The project is dedicated to developing and bringing to the pharmaceutical market an innovative gene-therapy medicinal product, «Genoterosil», aimed at accelerating bone tissue regeneration in osteogenesis imperfecta, skeletal dysplasias, osteoporosis, non- and delayed-union fractures, and pseudarthrosis.

1 Problem

Prolonged fracture healing times, the development of false joints (pseudarthrosis), and the risk of disability in cases of difficult-to-heal fractures.

2 Solution

Enhancing the expression of genes responsible for bone tissue formation will expedite osteogenesis, shorten patient immobilization time, and minimize the risk of complications.

Product and Its Advantages

Description

«Genoterosil» (soluble lyophilized powder for intramuscular injection) is a gene-therapy product for bone tissue regeneration. It contains recombinant DNA vectors bearing the genes for bone morphogenetic proteins (BMP-2, BMP-7) and type I collagen (COL1A1/A2), which promote stem cell migration and differentiation to the fracture site, regulate osteoblast–osteoclast activity, and increase the synthesis of extracellular matrix.

Indications for Use (according to ICD10):

- Fractures of the ulna and radius (S52)
- Fractures of the humerus and femur (S42, S72)
- Fractures of the tibia (S82)
- Nonunion of fractures (M84.1)
- Delayed fracture healing (M84.0)
- Malunion of fractures (M84.4)
- Other skeletal fractures (T02, future indication)
- Femoral neck fractures (S72.0, future indication)
- Dental applications (S02, K00–K08, future indication)

Product and Its Advantages

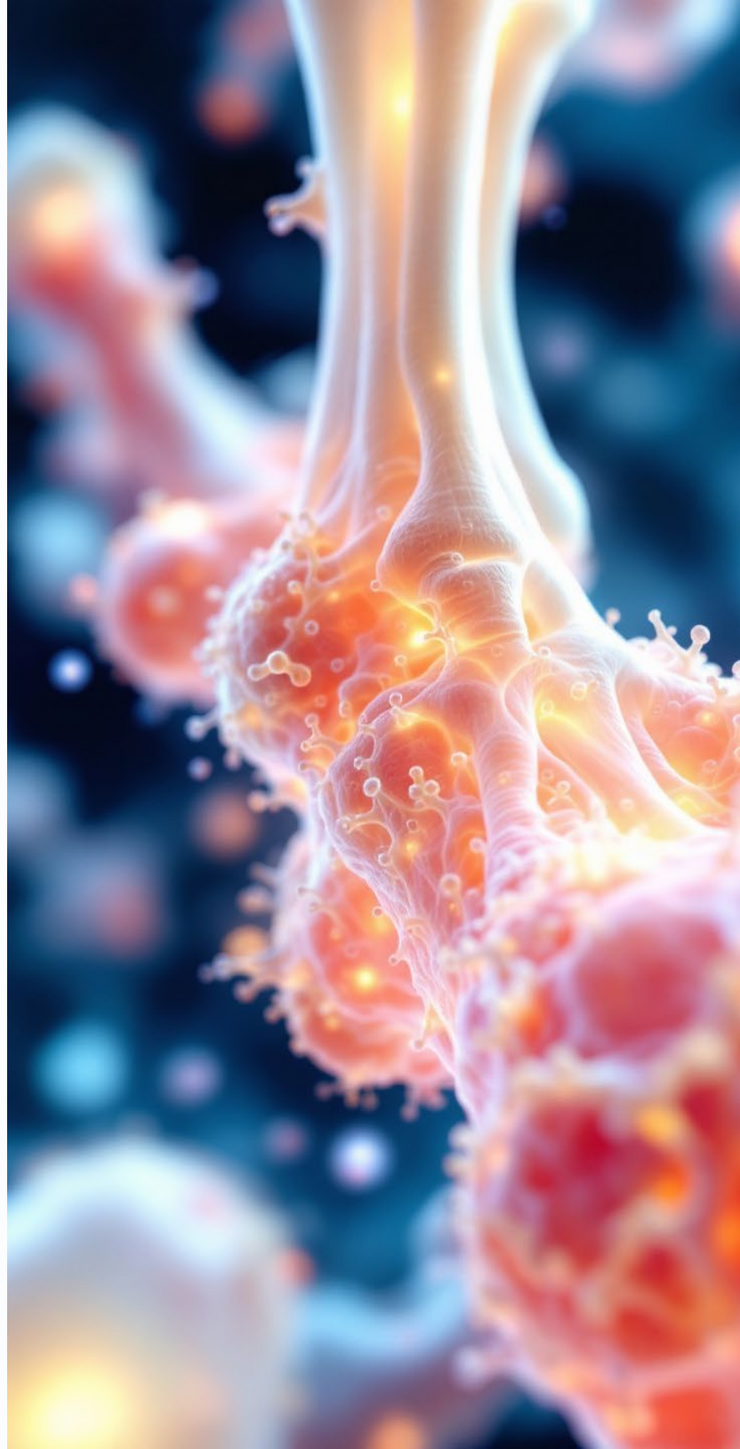
Efficacy

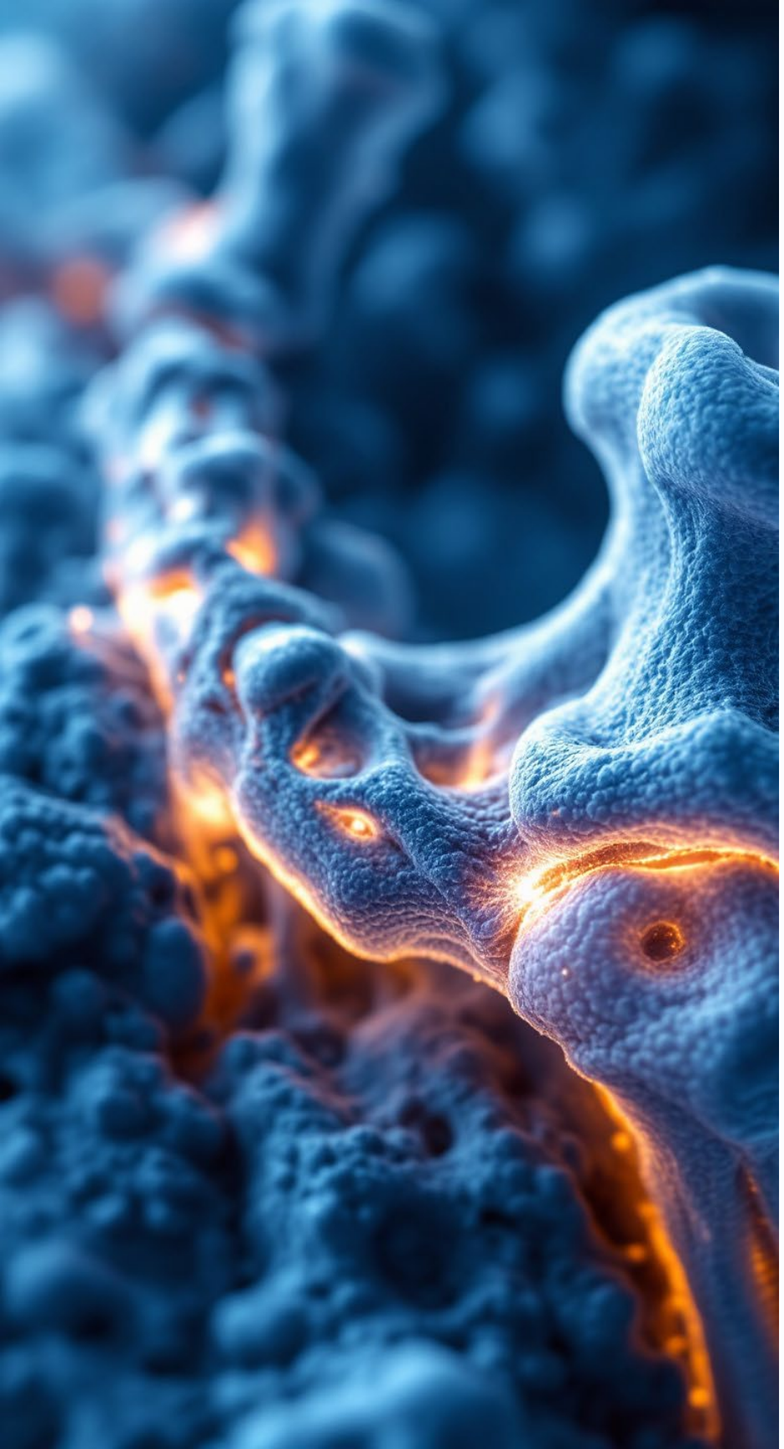
Use of Four Target Genes to Multiply the Therapeutic Effect. Incorporating four distinct genes in the formulation amplifies therapeutic impact by following multiple pathways involved in bone regeneration.

High-Efficiency Gene Expression. Achieved through regulatory elements within the DNA vectors that do not derive from viral genomes, thereby reducing safety concerns and maintaining targeted, robust protein production.

Calcium-Phosphate Precipitate as the Delivery System. Serving not only as a carrier for DNA vectors but also functioning as a “raw material” for mineralizing newly formed bone tissue.

Preclinical Studies Confirm Accelerated Osteogenesis. A comprehensive evaluation—using molecular-genetic, histological, immunohistochemical, radiographic, and biochemical methods in both cell cultures and animal models—has confirmed enhanced bone healing in hard-to-heal fractures.





Product and Its Advantages

Safety

No Genomic Integration and No Antibiotic Resistance Risk. DNA vectors do not integrate into the host cell genome, and the absence of antibiotic-resistance genes in the formulation prevents the emergence of resistant strains in patients.

Local Injection at the Fracture Site. Administering the product via direct injection into the fracture zone significantly reduces the systemic effects of morphogenetic proteins (e.g., ectopic ossification).

No Induction of Immune Response. Since there are no viral genome elements in «Genoterosil», the immune system remains unprovoked, preserving the potential for repeated administration without immunogenic complications.

Extremely Low Toxicity Demonstrated in Preclinical Studies. Classified as a low-hazard drug based on animal toxicity data; no gonadotoxic, allergenic, immunotoxic, or mutagenic effects were identified.

No Immunogenicity or Adverse Events in Phase I Clinical Trials. Healthy volunteer data confirm a high safety profile and validate the feasibility of multiple administrations.

Completed Project Stages

1 DNA Vector Development

A base DNA vector was created, along with therapeutic vectors derived from it. A dedicated delivery system was designed to facilitate vector uptake by target cells, and the FDF was established and approved.

2 Strain Deposition and Patent Protection

Original producer strains for large-scale DNA vector production were created and deposited in specialized depositories: NCIMB and VKPM. All necessary patent procedures were completed.

3 Manufacturing

Laboratory-scale and pilot manufacturing protocols were developed, and manufacturing has been set up at a GMP-certified facility, with the technology transfer process successfully validated.

4 Preclinical Studies

A full range of preclinical evaluations confirmed the product efficacy and maximum safety in animal models.

5 Clinical Trials

Initial testing in healthy volunteers in Phase I clinical trials showed a favorable safety profile, resulting in approval to proceed with a combined Phase II–III clinical trial program.

Intellectual Property

Invention Patents

Patents have been granted for the DNA vectors included in the drug composition (US 11,352,639 B2; ZL 201980073044.8; EP 3847259; RU 0002707537), fully protecting the underlying intellectual property.

Rights and Licensing

The plan allows for licensing and/or assignment of these IP rights to a joint project entity or an industrial pharmaceutical partner.

Access to Depositories

The producer strains have been deposited with the NCIMB and the VKPM, enabling the immediate production of DNA vectors upon authorization to access the strain banks.

Market Description and Size

The market introduction of the gene-therapy medicinal product «Genoterosil» is both timely and socially significant. According to aggregate data, fractures of the upper and lower extremities affect approximately 1% of the total population annually, and up to 15% of these may be challenging to heal. Pseudarthrosis develops in up to 10% of fracture patients (combined estimates), and 2–5% may become fully disabled. In the defined patent protection regions:

>25 million patients with bone fractures per year

USD 3,000–7,000 average direct treatment costs per fracture

>USD 200 billion cumulative economic loss from disability in patients with fractures

Prospects and Significance

Improving Quality of Life

The emergence of an innovative gene-therapy product designed to accelerate osteogenesis holds enormous potential for improving patients’ quality of life.

Economic Potential

This new paradigm in bone regeneration offers broad applicability in traumatology, orthopedics, surgery, dentistry, and related fields.

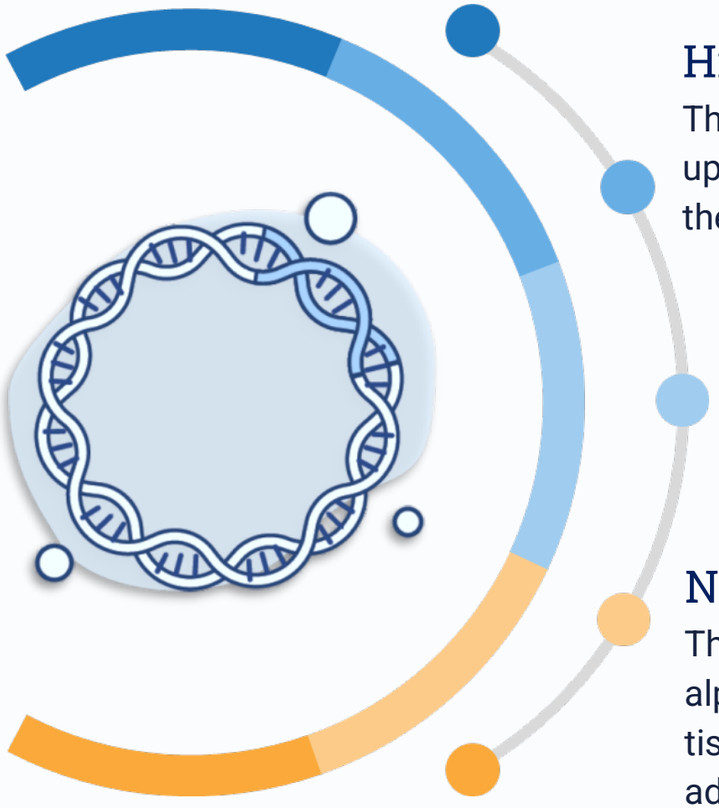
Scientific Contribution

A substantial contribution to the advancement of gene therapy and the development of novel medications for treating and preventing various diseases.

DNA-vector VTvaf17

Advantages

The VTvaf17 Non-Viral DNA Vector, on which «Genoterosil» is based, represents a next-generation, innovative DNA vector that integrates the advantages of multiple genetic delivery systems



Effectiveness

Minimal size - the VTvaf17 DNA vector measures only 3,165 base pairs, enabling effective transfection of various tissue cell types. The use of specifically selected promoters ensures precise targeting and high-level expression of therapeutic genes

High Production Yield

The manufacturing process for the VTvaf17 vector allows for yields of up to 200 mg of primary product per liter of bacterial culture, meeting the highest standards for technological efficiency

Absence of Antibiotic Resistance Genes

Vectors do not carry any antibiotic resistance genes, thus eliminating the risk of creating resistant strains in patients. Strain selection is enabled by the RNA-out regulatory element from the Tn10 transposon

No Viral Sequences

Therapeutic gene expression is driven by the human elongation factor 1 alpha (EF1A) promoter region, providing a high transcription rate in most tissues with no immunogenic response, and enabling repeated administrations without concern for viral components

Low Toxicity

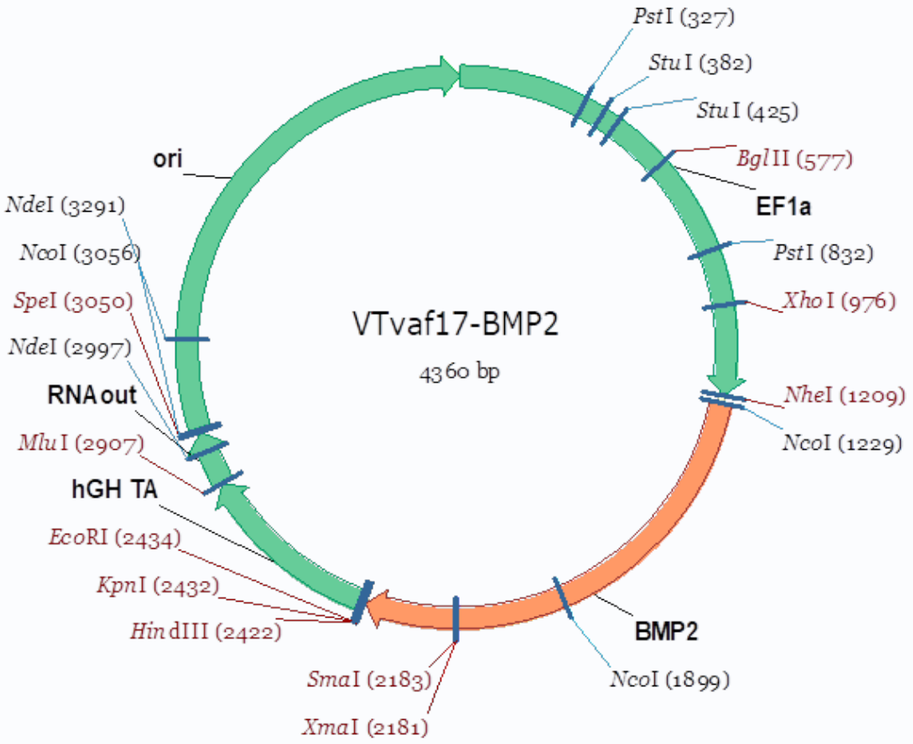
At the preclinical stage, the VTvaf17 DNA vector demonstrated extremely low toxicity across all study parameters

DNA-vector VTvaf17

Structure

«Genoterosil» is formulated as a mixture of DNA vectors carrying the human bone morphogenetic protein genes BMP-2 and BMP-7, as well as the collagen-encoding genes COL1A1 and COL1A2. Each DNA vector included in the product contains the following structural elements:

- EF1α - The promoter region of the human elongation factor 1 alpha (EF1A) gene, including its native enhancer located in the first intron. It provides a high level of recombinant gene transcription in most human tissues.
- cDNA of the Target Gene - The coding sequence of the desired gene (e.g., BMP-2, BMP-7, COL1A1, or COL1A2).
- hGH-TA - The transcription terminator and polyadenylation site from the human growth hormone (hGH) gene, used to ensure proper termination and stabilization of the transcript.
- RNA-out - A regulatory RNA-out element from the Tn10 transposon, enabling positive selection without antibiotics when using the Escherichia coli SCS 110 strain.
- Ori - The origin of replication (with a single-nucleotide substitution to boost plasmid copy number), allowing autonomous replication in most E. coli strains.



A schematic map of the VTvaf17-BMP2 DNA vector, which is part of the «Genoterosil» formulation

Thanks for watching!

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