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Grifols doses first patients in two Phase 3 trials to expand indications of its flagship immunoglobulins

- ***One trial, SIGMA, will evaluate Grifols' intravenous immunoglobulin (Ig) GAMUNEX®-C (immune globulin injection [human], 10% caprylate chromatography purified) plus standard medical treatment in patients with secondary immunodeficiency***
- ***A second trial, XPERT, will determine whether Grifols' subcutaneous Ig, XEMBIFY® (immune globulin subcutaneous human klhw) is non-inferior to GAMUNEX-C in patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)***
- ***Both studies are designed to support U.S. label expansion on these fast-growing Grifols Ig franchise therapies and offer patients more treatment options for their immune system disorders***

Barcelona, Spain, July 16, 2026 – Grifols (MCE:GRF, MCE:GRF.P, NASDAQ:GRFS), a global healthcare company and leading producer of plasma-derived medicines, today announced that the first patients have been dosed in two separate Phase 3 trials aiming to expand the U.S. labels for its signature immunoglobulin therapeutics, GAMUNEX®-C, an intravenous immunoglobulin (IVIg), and XEMBIFY®, its subcutaneous immunoglobulin (SCIg).

The SIGMA trial (NCT07582432) will evaluate the pharmacokinetics (PK), efficacy and safety of GAMUNEX-C in combination with standard of care treatment to prevent infections in patients with secondary immunodeficiency (SID) characterized by low immunoglobulin levels. Unlike primary immunodeficiency (PID), which is genetic, SID occurs when a person's previously healthy immune system is compromised by factors such as blood cancer and treatments like chemotherapy or B-cell-targeted therapies.

This trial will focus specifically on patients with common blood cancers including Chronic Lymphocytic Leukemia (CLL), Multiple Myeloma (MM) and Non-Hodgkin Lymphoma (NHL), which together account for more than 1 million patients in the U.S.[1] Expanding the label to include hematologic cancer–associated SID would broaden the approved indications for GAMUNEX-C in the U.S.

The second clinical trial, XPERT (NCT07540221) will determine if XEMBIFY's PK profile is non-inferior to that of GAMUNEX-C to treat patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP). It will also evaluate XEMBIFY's safety profile and efficacy based on its ability to keep the patients' condition under control. GAMUNEX-C is already indicated to treat this autoimmune disease. Favorable results showing non-inferiority between the two Ig therapeutics, which share similar manufacturing processes, may support future regulatory discussions, including a potential application to seek expansion of XEMBIFY's U.S. label to include CIDP.

[1] National Cancer Institute. SEER Cancer Stat Facts. Surveillance, Epidemiology, and End Results Program. Updated April 15, 2022. Accessed July 14, 2025.

About 60,000 patients in the U.S.[2] suffer from CIDP, a chronic illness, with symptoms including progressive weakness in the arms and legs and changes in sensation. Ig therapy, including GAMUNEX-C, is a first-line treatment with immunomodulatory properties that can improve neuromuscular disability and prevent relapse.

"The GBS I CIDP Foundation International embraces Grifols' commitment to innovate and to support the patient community with additional choice in treatment and access options," said Lisa Butler, president and CEO of The GBS | CIDP Foundation, which works to ensure the CIDP patient community has access to all necessary treatments at all points of care.

These two new trials aim to expand the U.S. indications of Grifols' Ig portfolio, adding to a third Ig trial already underway. Announced at the end of 2022, Grifols' EXCELL trial (NCT05645107) is a study to evaluate efficacy, safety, and PK of XEMBIFY+standard medical treatment (SMT) compared to placebo+SMT to prevent infections in participants with hypogammaglobulinemia (HGG) and recurrent or severe infections associated with B-cell Chronic Lymphocytic Leukemia, Multiple Myeloma, and Non-Hodgkin Lymphoma.

"We're excited about the potential to provide patients with more immunoglobulin treatment options to help manage their conditions with flexibility and convenience," said Eduardo Herrero, Grifols' Executive Vice President Biopharma Industrial and Scientific Innovation. "Whether it's our IVIg or SCIg treatments, Grifols' Igs are backed by decades of deep expertise on this protein."

Grifols' suite of Ig products to treat immune-system disorders continues to perform very strongly, driven by increasing patient need across the world. XEMBIFY, in particular, has benefited from robust demand, growing nearly 60% year over year in 2025.

About the new Phase 3 trials

The primary efficacy objective of the SIGMA trial is to demonstrate that the rate of serious bacterial infections is less than 1 per participant per year when treated with GAMUNEX-C plus standard of care medical treatment. Fifty participants will take part in the open-label, multicenter single-arm prospective study, all diagnosed with B-cell CLL, MM or NHL with hypogammaglobulinemia.

The XPERT trial is an open label, multicenter study that will evaluate the PK, efficacy and safety of XEMBIFY compared to GAMUNEX-C as maintenance therapy in approximately 40 CIDP patients across 20 sites in the U.S. and Europe.

This trial builds on the company's longstanding history of investing in CIDP research and treatment options for this patient community. In the mid-2000s, a pivotal trial centered on Gamunex-C — demonstrated its short-term and long-term efficacy in reducing disability, including improvement in grip strength, in patients with CIDP compared to placebo.

About GAMUNEX®-C in the U.S.

Indication
GAMUNEX-C (immune globulin injection [human], 10% caprylate/chromatography purified) is indicated for the treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years

[2] Arackal S, Venker C, Wang M, Schwinn J, Mina-Osorio P. Assessing the incidence and prevalence of chronic inflammatory demyelinating polyradiculoneuropathy in the United States: retrospective claims data analysis. Neurology. 2024;102(7 Suppl 1):P9-11.010. Published April 9, 2024. doi:10.1212/WNL.0000000000204780

of age and older, idiopathic thrombocytopenic purpura (ITP) in adults and children, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults.

Important Safety Information

Thrombosis may occur with immune globulin products, including GAMUNEX-C. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. For patients at risk of thrombosis, administer GAMUNEX-C at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IVIG) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IVIG products containing sucrose. GAMUNEX-C does not contain sucrose. For patients at risk of renal dysfunction or failure, administer GAMUNEX-C at the minimum concentration available and the minimum infusion rate practicable.

GAMUNEX-C is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin. It is contraindicated in IgA-deficient patients with antibodies against IgA and history of hypersensitivity.

Severe hypersensitivity reactions may occur with IVIG products, including GAMUNEX-C. In case of hypersensitivity, discontinue GAMUNEX-C infusion immediately and institute appropriate treatment.
Monitor renal function, including blood urea nitrogen (BUN), serum creatinine, and urine output in patients at risk of developing acute renal failure.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IVIG treatment, including GAMUNEX-C.

There have been reports of aseptic meningitis, hemolytic anemia, and noncardiogenic pulmonary edema (transfusion-related acute lung injury [TRALI]) in patients administered with IVIG, including GAMUNEX-C.
The high-dose regimen (1g/kg x 1-2 days) is not recommended for individuals with expanded fluid volumes or where fluid volume may be a concern.

Because GAMUNEX-C is made from human blood, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Do not administer GAMUNEX-C subcutaneously in patients with ITP because of the risk of hematoma formation.

Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of BUN and serum creatinine, before the initial infusion of GAMUNEX-C and at appropriate intervals thereafter.

Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies, because of the potentially increased risk of thrombosis.

If signs and/or symptoms of hemolysis are present after an infusion of GAMUNEX-C, perform appropriate laboratory testing for confirmation.

If TRALI is suspected, perform appropriate tests for the presence of antineutrophil antibodies and anti-HLA antibodies in both the product and patient's serum.

After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation.

In clinical studies, the most common adverse reactions with GAMUNEX-C were headache, pyrexia, hypertension, chills, rash, nausea, arthralgia, and asthenia (in CIDP); cough, rhinitis, pharyngitis, headache, asthma, nausea, fever, diarrhea, and sinusitis with intravenous use (in PIDD) and local infusion-site reactions, fatigue, headache, upper respiratory tract infection, arthralgia, diarrhea, nausea, sinusitis, bronchitis, depression, allergic dermatitis, migraine, myalgia, viral infection, and pyrexia with subcutaneous use (in PIDD); and headache, ecchymosis, vomiting, fever, nausea, rash, abdominal pain, back pain, and dyspepsia (in ITP).

The most serious adverse reactions in clinical studies were pulmonary embolism (PE) in 1 subject with a history of PE (in CIDP), an exacerbation of autoimmune pure red cell aplasia in 1 subject (in PIDD), and myocarditis in 1 subject that occurred 50 days post-study drug infusion and was not considered drug related (in ITP).

Please see full Prescribing Information for GAMUNEX-C or visit www.gamunex-c.com.

About XEMBIFY® in the U.S.

Indication

XEMBIFY® (immune globulin subcutaneous human–klhw) is a 20% immune globulin indicated for treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years of age and older. XEMBIFY is for subcutaneous administration only.

Important Safety Information WARNING: THROMBOSIS

- **Thrombosis may occur with immune globulin products, including XEMBIFY. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors**

- **For patients at risk of thrombosis, administer XEMBIFY at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk of hyperviscosity**

Contraindications

XEMBIFY is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin. It is contraindicated in IgA-deficient patients with antibodies against IgA and a history of hypersensitivity.

Warnings and Precautions

Aseptic meningitis syndrome (AMS). AMS may occur with human immune globulin treatment, including XEMBIFY. Conduct a thorough neurological exam on patients exhibiting signs and symptoms to rule out other causes of meningitis. Discontinuation of treatment has resulted in remission within several days without sequelae.

Thrombosis. Thrombosis may occur following treatment with immune globulin products, including XEMBIFY. Thrombosis may occur in the absence of known risk factors. In patients at risk, administer at the minimum dose and infusion rate practicable. Ensure adequate hydration before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk of hyperviscosity.

Hypersensitivity. Severe hypersensitivity reactions may occur with immune globulin products, including XEMBIFY. In case of hypersensitivity, discontinue infusion immediately and institute appropriate treatment. XEMBIFY contains IgA. Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions.

Renal dysfunction/failure. Acute renal dysfunction/failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis, and death may occur with use of human immune globulin products, especially those containing sucrose. XEMBIFY does not contain sucrose. Ensure patients are not volume-depleted prior to starting infusion. In patients at risk due to preexisting renal insufficiency or predisposition to acute renal failure, assess renal function prior to the initial infusion of XEMBIFY and again at appropriate intervals thereafter. If renal function deteriorates, consider discontinuation.

Hemolysis. XEMBIFY may contain blood group antibodies that may cause a positive direct antiglobulin reaction and hemolysis. Monitor patients for clinical signs and symptoms of hemolysis. If signs and symptoms are present after infusion, perform confirmatory lab testing.

Transfusion-related acute lung injury (TRALI). Noncardiogenic pulmonary edema may occur in patients following treatment with immune globulin products, including XEMBIFY. Monitor patients for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of antineutrophil and anti-HLA antibodies in both the product and patient serum. TRALI may be managed using oxygen therapy with adequate ventilatory support.

Transmissible infectious agents. Because XEMBIFY is made from human blood, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt- Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. No cases of transmission of viral diseases, vCJD, or CJD have ever been associated with the use of XEMBIFY.

Interference with lab tests. After infusion of XEMBIFY, passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation.

Adverse Reactions

The most common adverse reactions in ≥ 5% of subjects in the clinical trial were local adverse reactions, including infusion-site erythema (redness), infusion-site pain, infusion-site swelling (puffiness), infusion-site bruising, infusion-site nodule, infusion-site pruritus (itching), infusion-site

induration (firmness), infusion-site scab, infusion-site edema, and systemic reactions including cough and diarrhea.

Drug Interactions

Passive transfer of antibodies may transiently interfere with the immune responses to live attenuated virus vaccines (eg, measles, mumps, rubella, and varicella).

Please see accompanying full Prescribing Information for XEMBIFY or visit www.xembify.com

Globally, prescribing information varies; refer to the individual country product label for complete information.

About Grifols

Grifols is a global healthcare company founded in Barcelona in 1909 committed to improving the health and well-being of people around the world. A leader in essential plasma-derived medicines and transfusion medicine, the company develops, produces and provides innovative healthcare services and solutions in more than 110 countries.

Patient needs and Grifols' ever-growing knowledge of many chronic, rare and prevalent conditions, at times life-threatening, drive the company's innovation in both plasma and other biopharmaceuticals to enhance quality of life. Grifols focuses on treating conditions centered on six core therapeutic areas: immunology, neurology, pulmonology, hematology, hepatology and intensive care.

A pioneer in the plasma industry, Grifols continues to grow its network of donation centers, the world's most diversified with more than 400 across North America, Europe, Africa and the Middle East, and China.

As a recognized leader in transfusion medicine, Grifols offers a comprehensive portfolio of solutions designed to enhance safety from donation to transfusion, in addition to clinical diagnostic technologies. It provides high-quality biological supplies for life-science research, clinical trials and for manufacturing pharmaceutical and diagnostic products. The company also supplies tools, information and services that enable hospitals, pharmacies and healthcare professionals to efficiently deliver expert medical care.

Grifols, with more than 25,000 employees in more than 30 countries and regions, is committed to a sustainable business model that sets the standard for continuous innovation, quality, safety and ethical leadership.

The company's class A shares are listed on the Spanish Stock Exchange, where they are part of the IBEX-35 (MCE:GRF). Grifols non- voting class B shares are listed on the Mercado Continuo (MCE:GRF.P) and on the U.S. NASDAQ through ADRs (NASDAQ:GRFS).

For more information about Grifols, please visit www.grifols.com.

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