GRIFOLS

Grifols announces topline phase 3 data on long-term Albutein® (albumin [human] U.S.P.) therapy for decompensated cirrhosis with ascites

- ***Though primary endpoint of one-year transplant-free survival was not met, trial showed improved transplant-free survival, mortality and disease-related complications for patients treated with Albutein 20% plus standard medical treatment (SMT)***
- ***Improvement also observed in time-to-liver transplant or death at three months for the study treatment plus SMT patients, versus group receiving SMT alone***
- ***Long-term albumin dosing regimen demonstrated a favorable safety and tolerability profile with no adverse-reaction risks beyond what is already on label***
- ***Following further data evaluation, Grifols will present full results in H1 2025***

Barcelona, Spain, Dec. 20, 2024 – Grifols (MCE: GRF, MCE: GRF.P NASDAQ: GRFS), one of the world's leading producers of plasma-derived medicines, today announced topline data from its Phase 3 PRECIOSA clinical trial (NCT03451292) evaluating the potential of long-term albumin treatment with Grifols Albutein® on patients with decompensated cirrhosis and ascites.

Although the trial did not meet its primary endpoint of one-year transplant-free survival, an improvement in transplant-free survival, mortality and disease-related complications was observed for patients treated with Albutein 20% plus standard medical treatment (SMT) compared with patients receiving only SMT.

Further, a notable improvement in time-to-liver transplant or death at three months was observed for the study treatment plus SMT group of patients, when compared with the patients treated only with SMT. The safety and tolerability profile was favorable, and there were no adverse-reaction risks, beyond what is already on label, that would limit adoption of the therapy.

Trial participants benefited from albumin's antioxidant and anti-inflammatory properties, which are believed to mitigate the complications associated with decompensated cirrhosis.

Cirrhosis, a condition in which the liver is permanently scarred and can lead to liver failure, is the leading cause of liver-related deaths globally,[1] with more than 1.32 million deaths reported in

[1] GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* 2018;392(10159):1736-1788. doi:10.1016/S0140-6736(18)32203-7

2017.[2] In the U.S. alone, researchers estimate that about 1 in 400 adults have cirrhosis,[3] including those who have progressed into decompensated cirrhosis once complications such as ascites appear. Ascites is a buildup of fluid in the abdomen and signals that a patient's risk for poor outcomes, including death, have significantly increased.

"We believe that the improvement in transplant-free survival at three months is clinically meaningful for this patient population, especially considering the positive safety profile," said Dr. Jörg Schüttrumpf, Grifols Chief Scientific Innovation Officer. "Many patients with decompensated cirrhosis currently don't make it to transplantation due to the rapid progression of their disease into the next stage of acute-on-chronic liver failure (ACLF) and long wait times for a suitable transplant. We look forward to continuing to evaluate the full results and presenting them in H1 2025."

Grifols plans to present complete study results at the May 2025 EASL (European Association for the Study of the Liver) Congress.

The Phase 3 PRECIOSA trial evaluated the efficacy and safety of long-term Albutein administration (dosed every 10 ± 2 days for up to 12 months) plus SMT in over 400 patients with decompensated cirrhosis with ascites. It was a multi-center, randomized (1:1), controlled, parallel-group, open-label study taking place in 69 sites across North America and Europe.

Albutein is currently indicated in the U.S. for a broad variety of treatments including hypovolemia, cardiopulmonary bypass procedures, acute nephrosis, hypoalbuminemia, ovarian hyperstimulation syndrome, neonatal hyperbilirubinemia, adult respiratory distress syndrome (ARDS), and prevention of central volume depletion after paracentesis due to cirrhotic ascites. In Europe it is indicated for restoration and maintenance of circulating blood volume where volume deficiency has been demonstrated and use of a colloid is appropriate.

Global demand for albumin is growing and projected to reach $9.5 billion by 2030,[4] with China and the U.S. the two largest markets. The most abundant plasma protein in the body, albumin is used to replace lost fluids and restore vital blood volume. It is also utilized in treatments for conditions ranging from general and cardiac surgery to sepsis to cirrhosis.

Grifols in 2022 inaugurated a new albumin purification and filling plant in Dublin, Ireland, as part of a site expansion that tripled annual filling production capacity of its flexible container, ALBUTEIN FlexBag™, to further address rising demand for albumin. It comes in several sizes and concentrations and is the only product in its class with a 5% option.

The company is committed to advancing clinical practice and novel treatments with albumin and other biologics across a broad innovation pipeline. Its multiple plasma and non-plasma programs, spanning various clinical stages and therapeutic areas, are focused on developing potential treatments that help patients live longer lives.

---

[2] GBD 2017 Cirrhosis Collaborators. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol.* 2020;5(3):245-266. doi:10.1016/S2468-1253(19)30349-8

[3] Scaglione S, Kliethermes S, Cao G, et al. The Epidemiology of Cirrhosis in the United States: A Population-based Study. *J Clin Gastroenterol.* 2015;49(8):690-696. doi:10.1097/MCG.0000000000000208

[4] Marketing Research Bureau Report

GRIFOLS

About Decompensated Cirrhosis and Ascites

Chronic liver disease is an all too common and growing problem in the developed world, with worldwide prevalence rates of around 20%.[5] One such condition is cirrhosis, in which the liver is permanently scarred and, in many cases, can lead to liver failure. Decompensated cirrhosis is defined by the complications that can occur in a patient with cirrhosis, which include ascites, variceal bleeding, hepatic encephalopathy, and bacterial infections. These complications are associated with worse survival (2-4 years) compared with compensated cirrhosis (10-15 years).[6]

About Albutein

ALBUTEIN®, marketed in 5%, 20% and 25% presentations, is a sterile solution for single-dose intravenous administration containing 50g, 200g and 250 g per liter of total protein, respectively, of which at least 95% is human albumin.

Important Safety Information

ALBUTEIN® 5% (albumin [human] U.S.P.) is indicated for: hypovolemia, cardiopulmonary bypass procedures, hypoalbuminemia, and plasma exchange.

ALBUTEIN® 25% (albumin [human] U.S.P.) is indicated for: hypovolemia, cardiopulmonary bypass procedures, acute nephrosis, hypoalbuminemia, ovarian hyperstimulation syndrome, neonatal hyperbilirubinemia, adult respiratory distress syndrome (ARDS), and prevention of central volume depletion after paracentesis due to cirrhotic ascites.

ALBUTEIN 5% and 25% are contraindicated in patients with a history of hypersensitivity to albumin preparations or to any of the excipients, and in patients with severe anemia or cardiac failure with normal or increased intravascular volume.

Allergic or anaphylactic reactions require immediate discontinuation of the infusion and implementation of appropriate medical treatment.

Hypervolemia may occur if the dosage and rate of infusion are not adjusted to the patient's volume status. At the first clinical signs of fluid overload, the infusion must be slowed or stopped immediately. Use albumin with caution in conditions where hypervolemia and its consequences or hemodilution could represent a special risk to the patient.

The colloid-osmotic effect of human albumin 25% is approximately five times that of blood plasma. Therefore, when concentrated albumin is administered, care must be taken to assure adequate hydration of the patient. Patients should be monitored carefully to guard against circulatory overload and hyperhydration. Patients with marked dehydration require administration of additional fluids.

Concentrated (20% - 25%) human albumin solutions are relatively low in electrolytes compared to 4% - 5% human albumin solutions. Regularly monitor the electrolyte status of the patient and take appropriate steps to restore or maintain the electrolyte balance when albumin is administered.

---

[5] Moon AM, Singal AG, Tapper EB. Contemporary epidemiology of chronic liver disease and cirrhosis. Clin Gastroenterol Hepatol. 2020;18(12):2650-2666. doi: 10.1016/j.cgh.2019.07.060

[6] López-Sánchez GN, Dóminguez-Pérez M, Uribe M, Nuño-Lámbarri N. The fibrogenic process and the unleashing of acute-on-chronic liver failure. *Clin Mol Hepatol.* 2020;26(1):7-15. doi:10.3350/cmh.2019.0011; Fanali G, di Masi A, Trezza V, Marino M, Fasano M, Ascenzi P. Human serum albumin: from bench to bedside. *Mol Aspects Med.* 2012;33(3):209-290. doi:10.1016/j.mam.2011.12.002

Regular monitoring of coagulation and hematology parameters is necessary if comparatively large volumes are to be replaced. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets and erythrocytes).

Regularly monitor hemodynamic parameters during administration of ALBUTEIN 5% and 25% (albumin [human] U.S.P.).

ALBUTEIN 5% and 25% must not be diluted with sterile water for injection as this may cause hemolysis in recipients.

Albumin is a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for ALBUTEIN 5% or 25%.

The most serious adverse reactions with use of albumin are anaphylactic shock, heart failure and pulmonary edema. The most common adverse reactions are anaphylactoid type reactions. Adverse reactions to ALBUTEIN normally resolve when the infusion rate is slowed or the infusion is stopped. In case of severe reactions, the infusion should be stopped and appropriate treatment initiated.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see full Prescribing Information (U.S.) for ALBUTEIN FlexBag 5%, ALBUTEIN FlexBag 25%, ALBUTEIN vial 5% and ALBUTEIN vial 25%. People interested in prescriber information outside the U.S. should consult the equivalent information in their own countries.

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 is focused on treating conditions across a broad range of therapeutic areas: immunology, hepatology and intensive care, pulmonology, hematology, neurology and infectious diseases.

A pioneer in the plasma industry, Grifols continues to grow its network of donation centers, the world's largest with over 390 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 23,000 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, please visit www.grifols.com.

MEDIA **CONTACT:**

Media Press Office
media@grifols.com
Tel. +34 93 571 00 02

INVESTORS:
Investors Relations Department & Sustainability
inversores@grifols.com - investors@grifols.com
Tel. +34 93 571 02 21

LEGAL DISCLAIMER