Grifols announces positive topline phase 3 fibrinogen clinical trial results

- ***In the AdFIrst study, Biotest's fibrinogen concentrate (FC), BT524, met the primary endpoint, demonstrating its effectiveness in treating acquired fibrinogen deficiency (AFD) as equivalent to standard of care, while maintaining an excellent safety profile***

- ***Regulatory approval process in Europe and United States set to begin in Q4 2024. It would be the first FC approved for an AFD indication in the U.S. in a global market for AFD with an estimated potential of USD 800 million***

- ***This milestone is part of Grifols' robust innovation strategy, balancing internal and external investments to build a comprehensive and diversified portfolio***

Barcelona, Spain, Feb. 14, 2024 – Grifols (MCE: GRF, MCE: GRF.P NASDAQ: GRFS), one of the world's leading producers of plasma-derived medicines, today announced that Biotest's positive topline results from AdFIrst, its phase 3 clinical trial of its fibrinogen concentrate (FC), BT524, advance this potential treatment for acquired fibrinogen deficiency (AFD), an underserved growth market.

The FC from Biotest, a Grifols Group company, met the primary endpoint. It is as effective as standard of care in reducing intraoperative blood loss in patients with AFD, while also maintaining an excellent safety profile.

"This successful clinical trial is a significant stride towards a potential therapy that could contribute to the care of patients who experience severe blood loss during major surgery," said **Jörg Schüttrumpf**, Grifols Chief Scientific Innovation Officer.

AFD, which typically occurs during surgical procedures when there's insufficient fibrinogen to arrest bleeding, is commonly treated with cryoprecipitate (a plasma extract) or fresh frozen plasma, both containing fibrinogen.

The drawback is that they also contain other proteins and elements that aren't necessary, so large volumes are needed to ensure enough fibrinogen. Plus both need to be thawed in advance, time consuming when lives are at risk. FC, which is also used to treat AFD, is a precision medicine in which patients on the operating table immediately receive only what's essential to curtail hemorrhaging.

BT524 will likely enter regulatory authorization processes in Q4 2024 starting in Europe and the United States. It would be the first FC approved for an AFD indication in the U.S. in a global market with an estimated potential of USD 800 million.

Fibrinogen, a plasma protein produced in the liver, plays a key role in stopping blood loss and in wound healing. Grifols' experience with it to manage surgical bleeding includes the fibrinogen-based fibrin sealant the company launched five years ago.

"The positive results for Biotest's fibrinogen are an important milestone and strengthen a Grifols innovation strategy that's diversified across plasma and non-plasma, balanced between internal and external investments, and includes both shorter- and longer-term development cycles," said **Victor Grifols Deu**, Grifols Chief Operating Officer.

Detailed results of the trial will be presented later this year.

Biotest, a Grifols innovation driver

The acquisition of Biotest has significantly reinforced Grifols' access to plasma, as well as the company's pipeline and sales presence. Furthermore, it has provided new scientific and industrial capabilities, enabling improved revenue growth and margin expansion through the introduction of innovative plasma proteins.

The step forward in BT524's development comes in the middle of two other Biotest innovations that also highlight this company's increasing contributions to Grifols' profitable growth.

In late 2022, Biotest's new immunoglobulin (Ig) Yimmugo® entered the European market and is awaiting authorization to become available in the U.S. Another Biotest protein, trimodulin – a polyvalent immunoglobulin with IgM, IgA and IgG – is in two phase 3 clinical trials evaluating its efficacy and safety in patients with either community-acquired pneumonia (CAP) or severe community-acquired pneumonia (sCAP).

About Biotest's AdFIrst trial

The trial for Biotest's fibrinogen concentrate (FC), BT524, is known as AdFIrst (Adjusted Fibrinogen Replacement Strategy) was a prospective, active-controlled, multicenter phase 3 trial investigating the efficacy and safety of BT524 in patients with acquired fibrinogen deficiency. Patients who had high blood loss during planned spinal or abdominal surgery were randomized 1:1 to treatment with BT524 or cryoprecipitate/fresh frozen plasma (FFP). To evaluate the efficacy of BT524, further blood loss was compared between both treatment options. Further information about the trial design can be found at www.clinicaltrialsregister.eu (EudraCT number: 2017-001163-20).

The trial met its primary endpoint, demonstrating that Fibrinogen concentrate (BT524) is non-inferior to standard of care (SOC), in reducing intraoperative blood loss in patients with acquired fibrinogen deficiency undergoing planned major spinal or abdominal surgery. Mean blood loss measured in the two treatment groups were 1,444 mL in the BT524 group versus 1,735 mL in the SOC group, resulting in a reduction of blood loss of 291 mL in patients treated with fibrinogen concentrate.

About fibrinogen and fibrinogen deficiency

Fibrinogen is a blood clotting factor that is produced in the liver. It plays a key role in primary haemostasis (stopping blood loss from bleeding wounds) and wound healing. In case of a lack or shortage of fibrinogen the blood's ability to clot is impaired, which leads to a much greater risk of bleeding and delayed haemostasis.

The fibrinogen concentrate alternatives fresh frozen plasma (FFP) and cryoprecipitate contain variable amounts of fibrinogen and must be thawed prior to treatment. The defined amount of fibrinogen in the fibrinogen concentrate will allow a tailor-made, patient specific and highly effective therapy.

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 24,000 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.

In 2022, Grifols' economic impact in its core countries of operation was EUR 9.6 billion. The company also generated 193,000 jobs, including indirect and induced.

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.

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