Biotest AG
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Biotest
From Nature for Life

Developing game-changing immunoglobulins

Now ready for partnering, Biotest's IgM Concentrate could be a breakthrough therapy for patients with severe community-acquired pneumonia.

Severe community-acquired pneumonia (sCAP) is a life-threatening infection and one of the leading causes of death worldwide. Patients requiring ventilation in an intensive care unit are given antibiotics and supportive or stabilizing treatments in an attempt to avoid the development of sepsis, which leads to the breakdown of circulation and paralysis of the immune system. But the death rate for patients with sCAP is high: one-third of ventilated patients will die, and sepsis only increases that rate—it can reach 60% if septic shock occurs. These severely ill patients desperately need a life-saving product.

Enter Biotest AG, a midsized global pharmaceutical company that develops and markets human plasma protein products (immunoglobulins, coagulation factors and albumin) and therapeutic drugs for immune and hematopoietic diseases. The company specializes in clinical immunology, hematology and intensive care medicine, and also develops monoclonal antibodies for various indications such as systemic lupus erythematosus and multiple myeloma.

IgM Concentrate

Biotest's IgM Concentrate, an IgM-enriched polyvalent immunoglobulin preparation, could be the game changer for patients with sCAP.

Current immunoglobulin preparations on the market contain mostly IgG, the most prevalent antibody in the bloodstream. However, IgM antibodies act through a unique range of mechanisms thought to better counteract the pathophysiology of severe infections.

Through an innovative production process, Biotest is able to produce a natural and highly active immunoglobulin preparation that contains around 23% (mean) pentameric IgM. This IgM-enriched product exhibits more effective antibody activities than only IgG-containing products against various bacteria and their respective toxins by broadly binding pathogens, including drug-resistant strains. According to current understanding, adding IgM Concentrate to sCAP treatment supports therapy by neutralizing bacterial toxins, rebalancing the immune system and may reduce the risk for septic shock and organ failure, resulting in reduced mortality.

Clinical results to date have been remarkable. Findings from a recent randomized, placebo-controlled phase 2 study in severely ill intensive care patients with sCAP show that when IgM Concentrate is used as an adjunct treatment, it reduces relative mortality by more than half in patients showing signs of severe inflammation as detected by specific markers.

"The observed reduction of mortality is extraordinary," said Tobias Welte, coordinating investigator and head of pulmonology at Hannover Medical School. "A successful phase 3 trial would be a breakthrough therapy option in this field."

With the number of sCAP patients expected to reach 154,000 by 2025 in the United States alone, IgM Concentrate is an attractive market opportunity. Looking to further develop and market IgM Concentrate, Biotest is interested in partners willing to cofund phase 3 trials and commercialize the product in certain territories, including the United States.

Such promising results in sCAP mean Biotest may also develop IgM Concentrate for other indications. Potential additional areas are manifold and include other life-threatening diseases of high unmet need, such as multidrug-resistant infections, peritonitis, primary immunodeficiencies and organ-transplant related diseases. "We see a huge market potential for the product," said Joachim Herborg, executive VP commercial operations.

In addition to IgM Concentrate, Biotest has a range of products in development available for licensing and/or partnering (**Table 1**). Additional products in its pipeline include fibrinogen for bleeding disorders and polyspecific immunoglobulins for various immunological indications. The most advanced is Civacir, the only hepatitis C virus (HCV) immunoglobulin therapy in the world in an almost completed phase 3 trial to prevent HCV recurrence in liver transplantation. Positive data from an ongoing trial were presented at the 2015 meeting of the American Association for the Study of Liver Diseases, and preclinical analyses for other indications such as hepatocellular carcinoma and chronic HCV infection are under way.

Table 1 Biotest's pipeline programs for partnering

Therapeutic program	Status	Next clinical milestone	Candidate
Severe community-acquired pneumonia	Phase 2 finalized	Start of phase 3	IgM Concentrate
Hepatitis C	Phase 3 liver transplant study	Phase 3 completion	Civacir
Multiple myeloma	Phase 2 ongoing (in combination with Lenalidomide/ dexamethasone and pomalidomide / dexamethasone	Start of phase 3 and/or other combinations	Indatuximab ravtansine (ADC)
Solid tumor indications	Phase 1/2a ongoing (monotherapy)	Start of early combination studies (e.g., with checkpoint inhibitor)	
Systemic lupus erythematosus	Phase 2a	Interim data available by the third quarter of 2016	BT-063 (monoclonal anti-IL-10)
Immuno-oncology	In evaluation		

From plasma to patient

Founded in 1946 by Hans Schleussner, Biotest today has more than 2,200 employees and generated revenues of €589.6 million ($674 million) in 2015. The company has long-running experience in the field of infectious diseases and leads the market with specific immunoglobulins for hepatitis B, cytomegalovirus and varicella zoster.

Biotest's success lies in its wide-ranging experience and expertise, spanning plasma sourcing from collection centers across Europe and the United States, efficient high-quality manufacturing, preclinical and clinical R&D, marketing and worldwide distribution. "With IgM Concentrate and our long-term experience in infectious diseases, we are poised to significantly impact the treatment of sCAP and potentially other life-threatening infections," said Joerg Schuettrumpf, senior VP of corporate R&D.

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