Araclon Biotech
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Araclon Biotech advances in its innovative vaccine and diagnostic test for Alzheimer's

Presents results on ABvac40 and ABtest-MS studies at the AD/PD™ 2022 Conference in Barcelona

ABvac40:

- ***Meets the primary objectives on safety and efficacy of the first part of the phase II clinical study. Also confirms the vaccine's excellent safety and tolerability profile, as well as a strong immune response in patients with amnestic mild cognitive impairment (aMCI) or very mild Alzheimer's disease (vm-AD)***

- ***ABvac40 is based on an active immunization against the amyloid-beta 40 protein to fight early-stage AD***

ABtest-MS:

- ***Two studies confirm the test's ability to identify precisely those subjects with cerebral amyloid load, one of the first signs of early-onset AD***

- ***ABtest-MS, developed entirely in Araclon based on mass spectrometry, is capable of quantifying amyloid-beta 40 and 42 proteins – both associated with the risk of having AD – in plasma samples***

Zaragoza, Spain, March 15, 2022 - Araclon Biotech, a Grifols Group company dedicated to the research and development of therapies and diagnostic methods applied to degenerative diseases, will present topline results for the first part of its phase II clinical trial on its active immunotherapy, ABvac40, against Alzheimer's Disease (AD), as well as data on two studies of its assay, ABtest-MS, to identify early-stage AD.

Araclon will present its findings at the 16th International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders (AD/PD™ 2022), held March 15-20 in Barcelona.

Regarding the vaccine ABvac40, the principal data analyzed until now (Part A) are satisfactory in that they support the continuation of the trial's extension phase (Part B). Researchers have confirmed that the vaccine shows an excellent safety and tolerability profile, in addition to demonstrating a high immune response in patients with amnestic mild cognitive impairment (aMCI) or very mild AD[1].

"We are pleased to communicate these data at the international Conference *AD/PD™ 2022,* which confirm previous results on the safety and tolerability of ABvac40 in the early stages of

[1] *Update Phase 2 Study of ABVAC40, an active vaccine anti-AB40 in patients with mild cognitive impairment or very mild Alzheimer's Disease. Elisabet Molina, Sergio Castillo, Ana M. Lacosta, Jose A. Allué, Noelia Fandos, Judith Romero, María Montañés, Mª Leticia Sarasa, Jose Terencio, Mercè Boada on behalf of ABvac40 study group and Manuel Sarasa. CTAD 2021, Boston, November 9-12, 2021.*

Alzheimer's disease," said Jose Terencio, Araclon CEO and Vice President of Innovation at Grifols. "In addition the vaccine demonstrates that it induces a strong immune response characterized by the increase in anti-Aβ40 titers at the same time that Aβ40 levels rise in plasma. We are analyzing the results of the secondary variables (exploratory), related to efficacy, and we hope that ABvac40 shows its potential and lead to an innovative vaccine for patients."

This multicenter, random and double-blind phase II trial included a total of 124 patients with aMCI or very mild AD and were divided evenly between the treated group and the control group.

As far as the primary objective of safety, there were no significant differences between the participants in the group that received ABvac40 and those dosed with the placebo, including incidences of ARIA-H. No ARIA[2]-E events were reported during Part A of the study. These data confirm those obtained in phase I and presented in July 2016, which showed a good safety profile[3].

With respect to the other primary objective, efficacy (immunogenicity), the administration of six doses of ABvac40 resulted in a significant increase in the specific antibody levels, greater than those observed in the phase I trial (three doses).

This phase II evaluates as secondary efficacy variables (exploratory) changes in the disease's biomarkers, as well as in cognition and the quality of life resulting from ABvac40. The study's Part B is progressing according to plan.

Studies confirm the predictive potential of ABtest-MS for the early diagnosis of AD in heterogeneous cohorts with different clinical characteristics

In addition, Araclon Biotech continues with its research focused on the development of solutions to detect AD in its early stages. Diverse studies confirm the high predictive ability of its assay ABtest-MS to identify precisely those subjects with cerebral amyloid load, a sign of early-onset AD, which would enable management of the condition in its initial phases.

ABtest-MS, a novel and unique method developed entirely in Araclon and based on the mass spectrometry technique, is capable of accurately quantifying amyloid 40 and 42 proteins – both associated with the risk of having AD – in plasma samples.

The results to be presented at the AD/PD™ 2022 Conference are centered on two recent studies. Data from the trial conducted on the FACEHBI[4] cohort, obtained after two years of follow up, confirm the potential of the ABtest-MS to predict the cerebral amyloid load, an initial sign of AD, in individuals with subjective memory complaints (SMCs) and the potential that the analysis

[2] *Amyloid Related Imaging Abnormalities (ARIA)*

[3] *Pre-assay handling of peripheral blood samples for quantification of Aβ peptides is critical when a diagnostic use is intended. It has been described physical and biochemical cues affecting Aβ quantification in blood-derived samples, suggesting that differences in sample processing may result in variations in the quantification. Stringent standardization, but on tested practical grounds, is advisable. (araclon.com)*

[4] *The project Ace Healthy Brain Initiative (FACEHBI) is a study on the early detection of Alzheimer's designed and coordinated by Ace Alzheimer Center Barcelona in 2014. Specifically, an exhaustive medical follow up was conducted on 200 cognitively healthy people with memory loss.*

of these markers have as an indicator of how the condition evolves. The data corresponding to five years of follow up with the cohort are currently being analyzed.

In the second study, the multicenter A4 Study[5] carried out in 50 centers, the ABtest-MS predicted the cerebral deposit of the amyloid protein (measured by PET) in plasma samples from 731 subjects. It also confirmed the suitability of utilizing a centralized and extensively validated method such as this assay in these broad and heterogenous studies[6].

These data confirm other results previously obtained on more than 1,000 subjects in different AD stages from various international cohorts (BioFINDER, DPUK) that have been recently featured in scientific publications such as *Alzheimer's Research & Therapy*, *Nature Aging* and *Alzheimer's & Dementia: The journal of the Alzheimer's Association*, confirming the relation between amyloid biomarkers in plasma and AD.

"This test's predictive ability makes it ideal to detect early-stage Alzheimer's and accelerate the recruitment for clinical trials of new treatments, reducing the screening failure rate and associated costs," said Terencio.

ABtest-MS is a differentiating method that doesn't contain antibodies and whose process avoids enzymatic digestion, saving time and expense.

Access to communications and publications:

- **Access to ABtest-MS featured in *Alzheimer's Research & Therapy* here**
- **Access to ABtest-MS featured in *Nature Aging* here**
- **Access to ABtest-MS featured in *Alzheimer's & Dementia: The journal of the Alzheimer's Association* here**

The posters and the scientific presentation will be available beginning March 21 on Araclon Biotech's web

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[5] *El A4 Study (Anti-Amyloid treatment in Asymptomatic Alzheimer's disease) selected more than 5,000 healthy individuals between 65 and 85 years old that showed signs of having accumulated amyloid protein in the brain, demonstrated through PET images.*

[6] *Accurate discrimination of brain amyloid status in the multi.centric A4 study by plasma Aβ42/Aβ40 measured with a novel HPLC-MS/MS method. Leticia Sarasa, María Pascual-Lucas, José A. Allué, Sergio Castillo, María Eugenia Sáez, Sara Abdel-Latif, Robert A. Rissman, Jose Terencio and Manuel Sarasa. AD/DP 2022, Barcelona, March 15-20, 2022.*

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About Araclon Biotech

Araclon Biotech specializes in researching and developing therapies and diagnostic methods for Alzheimer's disease (AD) and other neurodegenerative diseases. The company, in which Grifols holds a stake of almost 76%, focuses on two research areas: the early diagnosis of AD by means of detecting amyloid-beta peptides in the blood, and the treatment of the disease using immunotherapy (vaccines).

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. Its four divisions – Bioscience, Diagnostic, Hospital and Bio Supplies – develop, produce and market innovative solutions and services that are sold in more than 110 countries.

Pioneers in the plasma industry, Grifols operates a growing network of donation centers worldwide. It transforms collected plasma into essential medicines to treat chronic, rare and, at times, life-threatening conditions. As a recognized leader in transfusion medicine, Grifols also offers a comprehensive portfolio of solutions designed to enhance safety from donation to transfusion. In addition, the company 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 30 countries and regions, is committed to a sustainable business model that sets the standard for continuous innovation, quality, safety and ethical leadership.

In 2021, Grifols' economic impact in its core countries of operation was EUR 7.7 billion. The company also generated 141,500 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