

## ExonHit presents promising data on genomic biomarkers in Alzheimer's disease clinical trials

- Aid in the selection of a homogeneous patient population to increase chances of successful study outcomes
- Identification of biomarkers to predict response to treatment or monitor efficacy

**Paris, France - November 8, 2010** - ExonHit Therapeutics (Alternext: ALEHT) announced today that promising data regarding the use of blood-based genomic biomarkers in Alzheimer's disease (AD) clinical trials were disclosed in two distinct oral presentations at the Third Conference of Clinical Trials on Alzheimer's Disease (CTAD) from November 3<sup>rd</sup> to November 5<sup>th</sup> in Toulouse, France.

The CTAD 2010 brought together current thought leaders involved in AD clinical trials to discuss in particular new results, new drug development, and methodological items (disease modifying outcomes, biomarkers, etc...).

To date, clinical trials designed to evaluate a new treatment for Alzheimer's disease select patients based on clinical criteria, using psychometric scales, brain imaging and measurements in cerebrospinal fluid. AD being a complex disease with multiple clinical manifestations, clinical trial results are sometimes difficult to interpret due to the heterogeneity of the patient population. Similarly, treatment response in AD is mainly assessed using psychometric scales with results that also vary according to the rater's experience or the patient's disposition.

*"Including the use of a simple blood-based molecular biomarker such as AclarusDx™ in Alzheimer's disease trials may facilitate the recruitment of a more homogeneous Alzheimer patient population and thus contribute to reduce random noise in trial results, hence making it easier to evaluate a drug's potential efficacy,"* stated Professor Serge Gauthier, M.D. from McGill University in Montreal. *"In addition, drawing blood from patients can be done almost anywhere and is much easier than collecting cerebrospinal fluid in an aged and fragile patient population."*

*"Thanks to the development of comprehensive profiling technologies such as our SpliceArray™ platform, pharmacogenomic analysis can be applied in clinical trials to develop predictive or monitoring biomarkers that can be used to identify patients who will benefit from a treatment or to follow their response to that treatment. This is what we have done with EHT 0202, our Phase II compound in Alzheimer's disease,"* added Matthew Pando, PhD, Executive Vice President, Therapeutics of ExonHit Therapeutics.

The oral presentation given by Professor Gauthier was entitled "How biomarkers can help investigators and the pharmaceutical industry in AD clinical trials. From concept to application" and described the different ways of considering the use of genomic biomarkers in AD clinical trials, in particular for patient selection, stratification and recruitment. Adding genomic homogeneity to the patient selection criteria could contribute to improving the study power to detect a real effect or, equivalently, reducing the number of patients needed to detect such an effect (1).

The EHT 0202 oral presentation by Matthew Pando entitled "Identification of blood transcriptomic signatures in AD patients related to EHT 0202 treatment response and efficacy" highlighted how a drug response can be correlated to genomic expression profiles. ExonHit's proprietary SpliceArray™ technology identified a potential blood-based transcriptomic signature specific to treatment response to EHT 0202 (2).

Both presentations underlined how the use of clinically relevant biomarkers could improve the chances of getting exploitable results when conducting AD trials. AD patients are a fragile population because of their age and of the associated pathologies; expanding the use of simple, non-invasive biomarkers in addition to current standard methods could significantly contribute to the successful development of new treatments for AD.

### **About AclarusDx™**

AclarusDx™ is a blood-based test to help in the diagnosis of Alzheimer's disease (AD). It detects transcriptomics biomarkers specific for AD in peripheral blood and is to be used in association with standard methods of assessments to help memory clinical experts in the diagnosis of AD. This test has been made available since December 2009 as a product for clinical research, in particular to optimize the selection of patients participating to therapeutic trials. It targets the market of pharmaceutical companies and university hospitals. CE mark is expected by the end of 2010 and launch in the *in vitro* diagnostic market is planned for Q1 2011 in France.

### **About EHT 0202**

EHT 0202 is ExonHit's lead candidate in Alzheimer's disease and potentially first in a new class of disease modifying therapies which stimulate the  $\alpha$ -secretase pathway, thus enhancing the production of the procognitive and neuroprotective sAPP $\alpha$  fragment of APP (Amyloid Precursor Protein). Since the stimulation of the  $\alpha$ -secretase pathway is to the detriment of A $\beta$  amyloid peptide production, EHT 0202 potentially reduces toxic A $\beta$  plaque formation (3). The compound successfully completed Phase IIa testing and efforts are ongoing to find a partner to continue its clinical development.

### **About ExonHit's SpliceArray™ platform**

ExonHit's SpliceArray™ platform is a novel generation of microarrays that incorporates a specific probe configuration, enabling an exhaustive monitoring of RNA splice variants (4). The Human Genome Wide SpliceArray™ biochips which profile close to 21,000 human genes associated to 140,000 RNA splice events have been used in the Company's biomarker discovery process.

RNA splicing represents a key regulatory mechanism of gene expression. One single gene can be transcribed into several splice variants encoding proteins exhibiting different biological functions. Current predictions suggest that as many as 80% of human genes exhibit some form of alternative splicing. Given the large contribution of splice variants to the human transcriptome and the high density of disease-causing mutations that occur in splicing-related sequences, the monitoring of alterations in alternatively spliced transcripts represents not only a source of potential drug targets, but also a biomarkers discovery engine.

### **About Alzheimer's disease**

Alzheimer's disease is a progressive neurodegenerative condition that is the most frequent cause of dementia in the elderly. It is a disease of multifactorial origin that involves environmental and genetic factors. Worldwide, an estimated 26.6 million people had Alzheimer's disease in 2006. This number is set to quadruple by 2050 to more than 100 million; 1 in 85 people worldwide will be living with the disease (5). In France alone, 800,000 people, or 18% of the population over-75, have Alzheimer's disease (6).

## **About ExonHit Therapeutics**

ExonHit Therapeutics (Alternext: ALEHT) is a fast emerging healthcare player active in both therapeutics and diagnostics. The Company is applying its proprietary technology, based on the analysis of alternative RNA splicing, to develop innovative molecular diagnostic tests and therapeutics for Alzheimer's disease and cancer indications. ExonHit has a balanced investment strategy with internal development programs and strategic collaborations, in particular with bioMérieux and Allergan.

ExonHit is headquartered in Paris, France and has U.S. offices in Gaithersburg, Maryland. The Company is listed on Alternext of NYSE Euronext Paris. For more information, please visit <http://www.exonhit.com>.

## **Disclaimer**

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*Finally, this press release may be drafted in the French and English languages. In an event of differences between the texts, the French language version shall prevail.*

## **References**

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