



PRESS RELEASE

Servier and Neurochlore join forces to treat autism in children

A partnership to accelerate the development of a medicine that could become the first treatment for the core symptoms of autism

14 March 2017 – Servier and Neurochlore announce today that they have signed an exclusive licensing agreement to develop and market bumetanide in pediatric autism in Europe.

The terms of the agreement state that Servier will develop and market the product in Europe and Neurochlore will retain these rights for the United States. Rights in relation to other countries are still under negotiation. The development plan includes three Phase 3 trials with an oral liquid form designed for children. Filing for marketing authorization is envisaged for the end of 2021.

Professor Ben-Ari has been studying bumetanide's mechanism of action for a number of years. In 2014, his research, published in *Science* magazine, demonstrated in animal models that it was possible to prevent autistic behavior in the offspring of females treated with bumetanide prior to giving birth. Bumetanide acts on the high chloride levels in neurons, which are observed in certain neurodevelopmental disorders such as autism, thus paving the way for research in humans. A Phase 2A clinical trial was first performed by Dr E. Lemonnier, then a Phase 2B multicentric trial was sponsored by Neurochlore in 6 centers in France including almost 90 children (from 2 to 18 years old). This study has recently produced promising results, published today¹, in favor of bumetanide based on several autism evaluation scales. An overall management of the disorder and particularly of its core symptoms of social deficit and repetitive behavior can thus be considered.

Prolonged use of bumetanide in children can be envisaged as it has many years of well-documented safety data among the adult population through its use to treat heart failure, as well as renal and hepatic edema.

Autism is a complex neurodevelopmental disorder affecting about one in 100 children, and is four times more prevalent in boys. Its cause remains unknown and no treatment exists to date. Management is purely symptomatic and involves individualized educational therapies.

« I am delighted that the research we have been pursuing for several decades on the development of ionic flows is going to lead to the treatment of a syndrome with no cure so far. It shows the importance of cognitive academic research and of collaboration with doctors and psychiatrists like Dr E. Lemonnier. I have always considered that experimental research should be centered on major concepts without prejudice to any medical treatment that, given time, could unexpectedly be developed, » declared Pr Yehezkel Ben-Ari, CEO of Neurochlore. « The understanding of the development of neuronal networks in pathological conditions thus paves the way to new therapeutic approaches of cerebral diseases, especially syndromes with intra-uterine origin. »

¹ Translational Psychiatry (2017) 7, e1056; doi:10.1038/tp.2017.10; published online 14 March 2017



Christian de Bodinat, Director of R&D for Neuropsychiatric disorders at Servier, concludes: *“We are enthusiastic about contributing to the development of a product that will potentially be the first treatment for the core symptoms of autism. This agreement illustrates our desire to focus our research on pathologies with very high medical need and to provide innovative therapeutic solutions to patients with neurodevelopmental disorders”.*

About Servier

Servier is an international pharmaceutical company governed by a non-profit foundation with its headquarters based in Suresnes (France). With a strong international presence in 148 countries and a turnover of 4 billion euros in 2016, Servier employs 21 000 people worldwide. Corporate growth is driven by Servier's constant search for innovation in five areas of excellence: cardiovascular diseases, diabetes, cancers, immune-inflammatory diseases, and neurodegenerative diseases, as well as by its activities in high-quality generic drugs. Being completely independent, the Group reinvests 25% of turnover (excluding generics) in research and development and uses all its profits for growth.

Servier has a solid commitment to neuropsychiatry and to proposing innovative therapies to patients suffering from neurological conditions. Its research teams are investigating new ways to treat Alzheimer's and Parkinson's diseases, as well as a broad range of neurodegenerative disorders, by targeting the toxic proteins that lead to neuron death. The priority is on focusing on the causes of the diseases rather than their symptoms. Currently, there are 5 projects at different stages of research and development in this promising area. This portfolio of innovative treatments is being developed with academic and biotech partners worldwide.

More information: www.servier.com

About Neurochlore

Created 5 years ago by Dr E Lemonnier, Nouchine Hadjikhani & Yehezkel Ben-Ari, Neurochlore is a biotechnology startup dedicated to determine molecular and cellular events occurring early in life in animal models of developmental disorders. Neurochlore is implanted within INMED an INSERM institute founded and previously directed by Y Ben-Ari thereby integrating basic and applied science considered essential to progress. Emertius Director at INSERM and CEO of Neurochlore Pr. Ben-Ari has received many awards including the grand prix of French and Belgian research as well as awards from American and European epilepsy foundations. Initially funded by Symmetry Capital (US), Neurochlore now employs 20 scientists (researchers and technicians). Neurochlore has conducted a phase 2A monocentric trial followed by a multicentric phase 2B trial (almost 90 children in 6 centers, France) with promising results. Neurochlore invests all its funding in basic science with no regard to potential applications, especially on developmental psychiatric or neurologic disorders that originate from a pathogenic event during pregnancy and/or delivery, or due to genetic mutations or environmental hazards. These pathologies are still poorly studied at a molecular and cellular level, and represent major public health issues.

More information: www.neurochlore.fr ,
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