Molecule for Fragile X Syndrome treatment receives orphan designation

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The European Medicines Agency (EMA) has granted "orphan designation" to BMS 204352, a molecule developed by the CNRS to treat Fragile X Syndrome, a rare genetic disease for which there exists no treatment. Protocol assistance will therefore be provided by the EMA to Dr Sylvain Briault at the Centre Hospitalier Régional in Orléans (west-central France) and his team at the Immunologie et Neurogénétique Expérimentales et Moléculaires laboratory - INEM (CNRS/University of Orléans) during the clinical development of the molecule.

Fragile X Syndrome is a genetic disease that causes inherited intellectual disability often associated with autism spectrum disorders as well as with characteristic physical signs. Affecting almost one in 4,000 infants, this is one of the most frequent rare diseases, but there is no existing treatment. Previous research led by Dr Sylvain Briault has shown that the combination of intellectual disability and autistic disorder is associated with abnormal activity of the BKCa potassium channel. In the case of Fragile X Syndrome, this channel is "normal" but half as common as in healthy subjects. BKCa was therefore identified by INEM researchers as a potential new therapeutic target.

The team tested molecule BMS 204352, and confirmed that it can open this channel. In addition, the molecule has already undergone a phase III clinical trial during which no toxicity was observed, prompting researchers to select it, even though its indication and administration route will be different than previously envisaged. Promising in vitro results led scientists to attempt in vivo tests on a mouse model carrying

Fragile X Syndrome. They observed that this molecule opens existing potassium channels widely and considerably increases their activity, making it equivalent to that of the controls. Consequently, the cognitive, emotional and social behavior of the mice with Fragile X Syndrome became similar to that of wild-type mice, used as controls in this study. In 2011, the CNRS, the University of Orléans and the Centre Hospitalier Régional in Orléans filed a patent on this molecule for the treatment of Fragile X Syndrome. It is being developed by FIST SA, a CNRS and BPI France technology transfer subsidiary. One of FIST SA's missions is to find industrial applications for novel technologies. This is the first step in a long research process and it does not guarantee potential results in humans.

This is the first orphan designation requested by the CNRS. The complex application process was made in close collaboration with FIST SA and the Fondation Maladies Rares, the French national body for coordinating and financing research into rare diseases. It received methodological support from OrphanDev/F-CRIN, the French national platform dedicated to clinical trials for rare diseases. A request will also be filed shortly with the FDA (Food and Drug Administration) to obtain orphan designation in the US.

This designation offers several advantages:

- free protocol assistance from the European Medicines Agency on conducting clinical trials and advising the applicant through the Marketing Authorization Application (MAA) process
- exclusive sales rights for 10 years in the European Union after obtaining the MAA, regardless of the duration of protection provided by the patent.

These advantages are especially useful when developing a drug, and finding pharmaceutical applications for it.

More information: Hébert et al.: "Rescue of fragile X syndrome phenotypes in Fmr1 KO mice by a BKCa channel opener molecule." *Orphanet Journal of Rare Diseases* 2014 9:124