Unité de recherche UMR_S1198
Mixte avec l'Université de Montpellier et l'EPHE
Mécanismes moléculaires dans les démences neurodégénératives
Tangui MAURICE, directeur

Dr Tangui Maurice
CNRS Research Director (DR1)

Tel. : +33/0 4 67 14 32 91
Email : tangui.maurice@umontpellier.fr

Montpellier, on May 24, 2023

Object : Lettre de soutien candidature ReST Therapeutics au prix Galien

Dear members of the Galien committee,
Dear colleagues,

I would like to express my full support for ReST Therapeutics' application for the Prix Galien. I am research director at the CNRS and director of the *Molecular Mechanisms in Neurodegenerative Dementia* laboratory (MMDN, UMR_S1198), placed under the triple supervision of the University of Montpellier, INSERM and EPHE. We have been hosting the ReST Therapeutics company in the laboratory for 2 years.

Within my team, we have been working on FENM for more than 3 years and we have been able to measure all the preclinical potential of the molecule. Through its unique mode of action, distinctly different from its parent molecule, memantine (Ebixa®), FENM proved to be very effective in the mouse models of Alzheimer's disease where we have studied it, including the pharmacological model of mice injected intracerebroventricularly with amyloid peptide oligomers or the transgenic mouse line overexpressing mutated human APP and presenilin 1 ($APP_{swe}/PS1^{\partial E9}$ line). The pharmacological model that we first used has proven predictive validity against transgenic models and has led, in our hands, to the discovery of at least four molecules that have subsequently shown chronic efficacy in transgenic models and allowed the tested molecules to enter clinical trials (e.g., blarcamesine, Neuro-EPO, Nuedexta, PXT3003). On this model and after chronic treatment for several months in the transgenic line, the evaluations already carried out have confirmed the remarkable efficacy of FENM over time, with a duration of action much longer than memantine, and qualitatively, in particular on neuroinflammation that is a primary factor in neurodegeneration. From a preclinical point of view , this molecule is one of the most promising that we have had the opportunity to study.

ReST Therapeutics is currently carrying out the analyses necessary to establish the molecule's IND file in order to launch phase I clinical studies as soon as possible. The company is also exploring, in collaboration with the laboratory of Christine Ann Denny at Columbia University in New York, the

potential of FENM as an atypical anxiolytic in indications of post-traumatic stress where the therapeutic arsenal is currently non-existent. The potential of this molecule is therefore remarkable and major in essential indications where the unmet medical need is glaring. Recognition of the work already accomplished would be a considerable lever for the dynamics of this young start-up with real potential.

I hope that you will give your full attention to the application of ReST Therapeutics.

Receive, dear colleagues, my best regards.

Tangui Maurice

MMDN, UMR_S1198
Université de Montpellier, INSERM, EPHE
cc 105, Place Eugène Bataillon
34095 Montpellier cedex 05 - France
Tél. : (+33/0) 4 67 14 33 86
Mel : secretariat.mmdn@umontpellier.fr

Institut national
de la santé et de la recherche médicale

École Pratique
des Hautes Études