

**IFB-088 (Sephin1) receives orphan drug designation in the European Union  
for the treatment of Charcot-Marie-Tooth disease**

**Nantes, France, January 25<sup>th</sup>, 2016.** InFlectis BioScience announces today that the European Commission has granted orphan drug designation to its drug candidate IFB-088, also known as Sephin1, for the treatment of Charcot-Marie-Tooth disease (CMT). This status provides specific incentives to InFlectis BioScience for the development of IFB-088, including assistance in the development of clinical protocols, royalties' exemptions from EMA and an exclusive ten-year marketing period in European Union.

CMT is one of the commonest inherited neurological disorders, affecting approximately 1 in 2,500 people. The disease affects the peripheral nerves, causing progressive weakness of the limbs, muscle wasting, deformities, and loss of sensation. It is caused by mutations or duplications in different genes that produce the proteins of the peripheral nerves. There is currently no effective treatment for CMT.

IFB-088 was granted orphan drug status for the treatment of CMT following a favorable review of preclinical data presented by the company to the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA). Its IFB-088 drug candidate has performed exceptionally well in two validated animal models of CMT subtypes: CMT1A and CMT1B which accounts for approximately 50% of all CMTs. Given orally after disease onset, IFB-088 completely restored the motor function of the CMT1A rats and CMT1B mice, suggesting considerable clinical potential. The study of the CMT1B mice was recently published in *Science* (Das *et al.* 2015, Vol. 348 p239) and showed that IFB-088 (named Sephin1 in the article) increased myelin thickness around axons in the sciatic nerves.

InFlectis BioScience and UK's Medical Research Council (MRC) are the co-owners of patent applications for the use of IFB-088 (Sephin1) in the treatment of CMT, for which InFlectis BioScience has executed an exclusive worldwide license of exploitation with the MRC.

*"IFB-088 orphan drug designation for the treatment of CMT will allow InFlectis to benefit from EMA's assistance in developing the clinical protocols currently under preparation and to benefit from the experience of regulatory authorities for our clinical development strategy in Europe "* said Philippe GUEDAT, PhD, Chief Executive Officer of the company.

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## Notes for editors:

### 1. ABOUT IFB-088 (also known as Sefpin1)

IFB-088 is a first-in-class orally available small molecule drug candidate with a validated mechanism of action and a promising pharmacokinetic profile for targeting the central and peripheral nervous system. IFB-088 is a selective inhibitor of PPP1R15A (GADD34), a stress-induced PP1 phosphatase regulatory subunit involved in the unfolded protein response. PPP1R15A inhibition by IFB-088 regulates the protein translation rate in stressed cells to a level manageable by the available cellular proteins that assist in protein folding (so-called “chaperones”), thereby restoring proteostasis. IFB-088 is strikingly specific for stressed cells, avoiding persistent inhibition of protein synthesis in normal, non-stressed cells.

### 2. ABOUT ORPHAN DRUG DESIGNATION

The European Orphan Drug status is granted to drug candidates for the treatment of life-threatening or chronically debilitating conditions affecting no more than 5 in 10,000 people in the European Union. In this context, pharmaceutical companies may find it difficult to cover their R & D investments by only subsequent sales. Obtaining the Orphan Drug designation provides certain benefits to the applicant, such as assistance in the development of clinical protocols, a centralized marketing authorization procedure (AMM), some fees exemption from European Medicines Agency and finally a marketing exclusivity period of ten years subject to obtaining an AMM.

### 3. ABOUT CHARCOT-MARIE-TOOTH DISEASE

Charcot-Marie-Tooth disease (CMT), named for the three doctors who first described it, is one of the commonest inherited neurological disorders. Also known as hereditary motor and sensory neuropathy (HMSN) or peroneal muscular atrophy (PMA), the disease comprises a group of disorders that affect both motor and sensory peripheral nerves. The age of onset and associated disability vary widely, from a mild impairment of gait and balance in adulthood to a childhood requirement for a wheelchair. Symptoms usually begin before the age of 20 years, and include clumsiness, leg weakness, fatigue, and foot drop together with typical deformities that include unusually higharched feet, hammer toes, and wasting of the lower legs. Nerve and muscle pains, decreased sensation, difficulty with mobility and balance, and wasting of hand muscles commonly occur.

CMT is classically divided into two major types, a demyelinating form (CMT1 and CMT4) and an axonal form (CMT2). CMT3, also known as Dejerine–Sottas syndrome, is a severe type of CMT in which symptoms begin in infancy or early childhood. An X-linked variant also occurs (CMTX). Approximately 60% of all CMT patients have CMT1, which is predominantly demyelinating. About 70% of these patients have CMT1A, which is associated with an autosomal dominant 1.4 MB duplication on chromosome 17p11.2 that includes the peripheral myelin protein 22 gene (PMP22) expressed predominantly in the compact myelin of Schwann cells. Another 5-10% of CMT1 cases have CMT1B which is associated with mutations in the major myelin protein zero gene (MPZ). The CMT1A subtype is by far the most common form of CMT, followed by CMT1X, CMT1B and CMT2A. Together these four subtypes account for more than 85% of all genetic diagnoses in CMT.

### 4. ABOUT MEDICAL RESEARCH COUNCIL ([www.mrc.ac.uk](http://www.mrc.ac.uk))

The Medical Research Council has been at the forefront of scientific discovery to improve human health. Founded in 1913 to tackle tuberculosis, the MRC now invests UK taxpayers' money in some of the best medical research in the world across every area of health. MRC-funded scientists tackle some of the greatest health problems facing humanity in the 21st century, from the rising tide of chronic diseases associated with ageing to the threats posed by rapidly mutating micro-organisms. "

### 5. ABOUT INFLECTIS BIOSCIENCE ([www.inflectisbioscience.com](http://www.inflectisbioscience.com))

InFlectis BioScience aims to discover and develop new molecules for the treatment of protein misfolding diseases. The company plans to demonstrate the clinical effectiveness of its candidate IFB-088 in humans, then partner with a pharmaceutical company for its subsequent development and commercialization. Meanwhile the company continues to develop new chemical series for the treatment of non-orphan diseases whose etiology also lies in the accumulation of misfolded proteins. Based in Nantes in the west of France, InFlectis BioScience is supported by Atlanpole ([www.atlanpole.com](http://www.atlanpole.com)), the Science and Technology Park of the Nantes Atlantique economic area.