PRESS RELEASE

InFlectis BioScience

Innovative therapeutics to treat protein misfolding diseases

FDA grants orphan drug designation to IFB-088 (Sephin1) for the treatment of Charcot-Marie-Tooth disease

Nantes, France, October 27th, 2015. InFlectis BioScience announces today that the US Food and Drug Administration (FDA) has granted orphan drug designation to the InFlectis BioScience drug candidate IFB-088, also known as Sephin1, for the treatment of Charcot-Marie-Tooth disease (CMT). The status confers several commercial advantages on InFlectis BioScience, including an exclusive seven-year marketing period for the drug, exemption from FDA application fees, and tax credits for clinical trials.

CMT is one of the commonest inherited neurological disorders, affecting approximately 1 in 2,500 people. It is estimated that approximately 128,000 people suffer from the disease in the United States. 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.

InFlectis BioScience's drug was granted orphan status in CMT after the FDA's review of the pre-clinical data submitted by the company, which specializes in the degenerative diseases caused by protein misfolding. Its IFB-088 drug candidate has performed exceptionally well in two validated animal models of CMT subtypes: CMT1A, which accounts for 40 to 50% of all CMT, and CMT1B. 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.

"We are delighted to receive FDA orphan drug designation for IFB-088 in CMT. This is an important milestone for the company and a significant step forward in our US and European clinical development strategy for IFB-088," said Philippe GUEDAT, PhD, Chief Executive Officer of the company.

"We believe IFB-088 is a highly promising treatment for CMT patients. Its novel mechanism of action, which targets the initiation step of protein synthesis in cells involved in the myelination process, means that our drug may be effective in different CMT subtypes, and possibly even other demyelinating diseases," said Pierre MINIOU, PhD, MBA, Chief Business Officer of InFlectis BioScience.

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Notes for editors:

1. ABOUT IFB-088 (also known as Sephin1)

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 FDA's Office of Orphan Drug Products grants orphan drug designation to support the development of medicines for under-served patient populations or rare disorders that affect fewer than 200,000 people in the United States. In both situations pharma companies may find it difficult to recover R&D costs from subsequent sales alone. Obtaining orphan drug designation confers certain commercial advantages on the applicant: InFlectis will enjoy an exclusive seven-year marketing period, be exempt from FDA application fees, and obtain tax credits for clinical trials.

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 INFLECTIS BIOSCIENCE (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), the Science and Technology Park of the Nantes Atlantique economic area.