



## Press Release

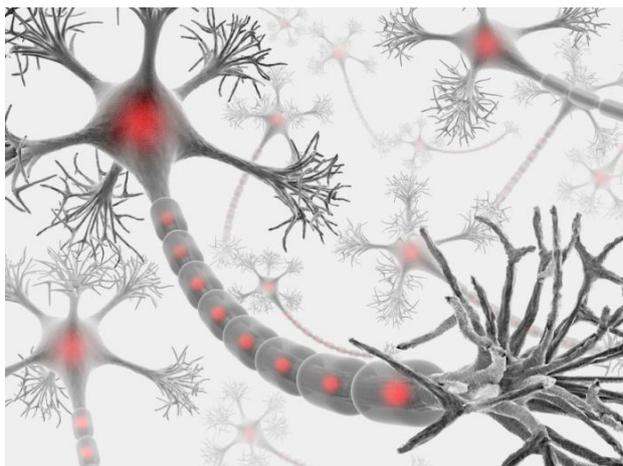
### **The Charcot-Marie-Tooth Association Enters Collaboration with Affectis to Advance Therapies for Charcot-Marie-Tooth 1A Disorder**

Dortmund/Chicago, 21 April, 2015 – The Charcot-Marie-Tooth Association (CMTA) announced today that it has entered into a collaboration with Affectis Pharmaceuticals AG to evaluate the efficacy of advanced Affectis compounds in neurological and behavioral models of CMT1A.

Affectis is a therapy development company and since 2013 a fully owned subsidiary of the Lead Discovery Center GmbH (LDC), a spin-off of Max Planck Innovation GmbH. The goal of the collaboration is to evaluate the pharmacology of small molecule antagonists of the P2X7 ligand-gated ion channel that are being jointly developed by Affectis and the LDC. P2X7 is an ATP-gated ion channel which is essential for cellular calcium homeostasis, and for the maturation and release of pro-inflammatory cytokines, including interleukin-1beta (IL-1 $\beta$ ).

The collaboration's aim is to demonstrate the potential of P2X7 antagonists that have high potency for the human form of P2X7 and are orally bioavailable in treating CMTA1. Use of such antagonists may impede the development of motor and sensory control defects associated with progression of the disease.

Pre-clinical studies previously demonstrated a likely role for P2X7 over-activity in the pathogenesis of CMT1A (Nobbio et al. (2009) J. Biol.Chem. 284, 23146). An altered calcium homeostasis was observed in Schwann cells from rats that exhibit a CMT1A pathology due to the expression of extra copies of the pmp22 gene; this is hypothesized to lead to the disruption of myelination associated with the disease. The authors further showed that the changes in intracellular calcium coincided with overexpression of the P2X7 ligand-gated ion channel, and that its inhibition leads to myelin repair.



*Charcot-Marie-Tooth disease Type 1 (CMT1) is rare inherited disorder of the peripheral nervous system characterised by progressive and severe demyelination.*

Patrick Livney, CEO of the CMTA notes: "The association has assembled the scientific and clinical key opinion leaders in CMT disorders and the research tools necessary to validate therapeutic opportunities for their clinical potential. We have set out to engage drug makers to work together with the CMTA to advance new therapeutic approaches to our patients, and our STAR network combines



this world class research expertise with an operational capability has been highly enabling to collaborative alliances formed for this purpose. Currently, there are no therapies for the different CMT disorders to halt either the onset or progression of the disease. This Affectis collaboration represents an exciting new opportunity for the CMTA to both de-risk and accelerate development of a novel drug class for the treatment of CMT1A, the most prevalent of the genetic neuropathies.”

Affectis CEO Michael Hamacher said of the collaboration: “Our P2X7 lead compounds have excellent pharmacological properties and repeatedly showed efficacy in various animal models. With initiation of the CMT1A studies we see the unique chance to evaluate both the role of P2X7 as well as the potency of the Affectis’ compounds in the Charcot-Marie-Tooth 1A disorder, a demyelinating neuropathy with unmet medical need. We are very much looking forward to the collaboration with the excellent team of experts from the CMTA to jointly progress the P2X7 leads into an effective therapy for Charcot-Marie-Tooth 1A”.

### **About Charcot Marie Tooth Disease Type 1A (CMT1A)**

CMT1A is a rare (1:5,000) hereditary motor and sensory demyelinating peripheral neuropathy (also known as Hereditary Motor and Sensory Neuropathy, HMSN) which is caused by an intrachromosomal duplication and consecutive toxic overexpression of the PMP22 gene on chromosome 17. CMT1A is one of the most common inherited peripheral nerve-related disorders passed down through families in an autosomal dominant fashion. CMT1A disease becomes evident in young adulthood and slowly progresses with distally pronounced muscle weakness and numbness. Pain can range from mild to severe. The disease can be highly debilitating with patients becoming wheelchair-bound and is often accompanied by severe cases of neurological pain. There is no known cure for this incapacitating disease.

### **About the Charcot-Marie-Tooth Association**

The Charcot-Marie-Tooth Association (CMTA) is a registered 501c3 dedicated to serving an international patient community that suffers from rare and disabling neuropathies of genetic origin. The CMTA directly engages its STAR scientific and clinical research network in the identification, validation and clinical development of therapies for the different Charcot-Marie-Tooth disorders.

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### **About Affectis and the LDC**

Affectis Pharmaceuticals AG is a pharmaceuticals company that develops novel drugs for the treatment of neurodegenerative and neuroinflammatory diseases. Affectis' capabilities in drug discovery and medicinal chemistry allowed the company to develop drugs with innovative mechanisms of action based on pioneering findings in the field of P2X7 receptors. Affectis started operations in January 2004 as a spin-off from the Max Planck Institute of Psychiatry. Since January 2014 Affectis



has relocated to Dortmund, Germany, and is now fully owned by and closely collaborates with the Lead Discovery Center GmbH (LDC) to further advance its core asset AFC-5128.

LDC was established in 2008 by the technology transfer organization Max Planck Innovation as a novel approach to capitalize on the potential of excellent basic research for the discovery of new therapies for diseases with high medical need. LDC is a translational incubator for innovative academic projects in the field of small molecule drug discovery and has a strong track record in successful industry partnerships with AstraZeneca, Bayer, Merck Serono and Daiichi Sankyo.

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