

Research Consortium led by Grünenthal receives €2 million grant from the European Fund for Regional Development and the State of North Rhine-Westphalia

- **“LifeSciences.NRW” grant to support the discovery and development of new pain relief drugs**
- **Grünenthal founded and leads the Consortium to which Taros Chemicals and the Research Centre Jülich belong**

Aachen, Germany, November 16, 2017 – Many patients who suffer strong or persistent pain receive inadequate relief from therapy. Improving pharmacotherapy and management for refractory pain is a so enormously complex problem that only concerted approaches which link together groups with different relevant expertise are likely to have success in discovering and developing novel and effective analgesics. Grünenthal, aiming at driving new solutions in pain, organized and leads such a partnership with three research groups from the Institute for Neurosciences and Medicine (INM) of the Research Centre Jülich, and with Taros Chemicals, a firm specialized in chemical design and synthesis. Together they designed an ambitious project which could pave the way to analgesic drugs with novel dual modes of action which target causes of refractory pain. This project is entitled „Development of PET-ligands to demonstrate the duality of the mechanisms of action of new analgesics” (Dual²PET).

LifeSciences.NRW is responsible for overseeing that European and regional development funds for the State of North Rhine-Westphalia are used to support this cooperative public-private partnership strategy with non-dilutive research grants. The Dual²PET research proposal was submitted to LifeSciences.NRW, and against strong competition from other North Rhine-Westphalian partnerships, won a research grant. The project will receive €2 million over three years from the European Funds for Regional Development and the State of North Rhine-Westphalia (Reference number EFRE-0800988), and started on 1st July 2017. Approximately 20% of all Europeans suffer from chronic, long-lasting or recurring pain, and 60% of these patients cannot be adequately treated with currently available medications¹. This situation causes enormous suffering to both the patients and their families.

Improved therapies for chronic pain will require highly innovative approaches which preferentially allow more than one pathological mechanism – mechanisms which cause diseases – to be influenced beneficially and simultaneously. Drugs which have more than one mechanism of action interact with more than one pharmacological target (“multiple ligands”). However, identifying such ligands is extremely difficult, and their transfer from preclinical research to clinical practice has been unsuccessful. The unsolved problem is to prove that candidate multiple ligands actually modulate simultaneously their multiple targets in animals and humans.

One possibility to prove the interaction of a new ligand with its targets is to employ newly developed imaging techniques such as positron-emission tomography (PET). This technology is employed in nuclear medicine to investigate and quantitate biological processes in a non-invasive and repeatable manner. The Dual²PET Consortium led by

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Grünenthal aims to develop a unique method whereby it will become possible to demonstrate the interaction of a single drug with two specific targets.

A method which allows such promising multiple ligands to be designed and then tested whether the pharmacological properties can be proven, first in animals and then in humans (Translational Medicine), would represent an enormous improvement for pharmaceutical research and development. Complex clinical developments would only be initiated after demonstrating a reasonable chance that a candidate has the desired properties. The Dual²PET approach is a paradigm shift which could save costs lost due to inadequate efficacy of candidates in clinical trials, and enhance the success rates by excluding candidates which lack promise, and thus provide patients with improved therapies more quickly.

About the Consortium

The scientific and technical challenges of this project are very complex, and can only be solved by an interdisciplinary team with extensive and complementary experience: Research at Grünenthal investigates pathological mechanisms which lead to pain in order to develop analgesics with improved properties. One focus is to employ innovative methods which promise an improved rate of translation from preclinical research into successful clinical practice, and so reduce the high attrition rate in clinical trials. The Dual²PET project will expand the research network and strengthen the science of Grünenthal's pain research.

Taros Chemicals is a small-to-medium sized enterprise (SME) with wide experience with organic and metallo-organic chemical syntheses. They use their state-of-the-art infrastructure and hardware to tackle complex synthesis and analysis techniques to apply a wide spectrum of computer-assisted drug design methods such as molecular modeling, virtual screening, adaptive structure-activity analyses and statistical prognoses.

The Research Centre Jülich involves itself in the Dual²PET project through three of its Institutes for Neurosciences and Medicine, "Molecular organization of the brain" (INM2), "Nuclear chemistry" (INM-5) and "Computational biomedicine" (INM-9/IAS-5).

They will investigate structural and functional changes in neurological and psychiatric diseases in order to improve early diagnosis and therapy. A central research focus will be the application of quantitative molecular imaging techniques such as positron-emissions tomography.

The consortium looks forward to the ground-breaking results from this pain project in the next years.

About the Leitmarktwettbewerb "LifeSciences.NRW"

The State of North Rhine-Westphalia created the competitive granting body LifeSciences.NRW in 2015 in order to support the development of solutions to problems of health and welfare in the aging population. Consortia of academic institutions, SMEs and pharmaceutical companies in NRW were offered the opportunity to compete for financial support of innovative biomedical research and development projects provided by the European fund for regional development. The intention is to strengthen growth and employment in NRW, and increase its visibility as a leading location for the life sciences.

About Grünenthal

The Grünenthal Group is an entrepreneurial, science-based pharmaceutical company specialized in pain, gout and inflammation. Our ambition is to deliver four to five new products to patients in diseases with high unmet medical need by 2022 and become a € 2 bn company. We are a fully integrated research & development company with a long track record of bringing innovative pain treatments and state-of-the-art technologies to patients. By sustainably investing in our R&D above the industrial average, we are strongly committed to innovation.

Grünenthal is an independent, family-owned company headquartered in Aachen, Germany. We are present in 32 countries with affiliates in Europe, Latin America and the US. Our products are sold in more than 155 countries and approx. 5,500 employees are working for the Grünenthal Group worldwide. In 2016, Grünenthal achieved revenues of approx. € 1.4 bn.

More information: www.grunenthal.com

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About Taros Chemicals

Taros Chemicals, a privately owned CRO / CMO has been serving the needs of pharmaceutical, chemical and biotech companies since 1999. More than 10.000 synthesis, research and process chemistry projects have successfully been delivered to the global customer base. Taros' scientists combine more than 140 years industrial organic chemistry experience and over 60 years of active drug discovery experience. They have expertise in major therapeutic areas and in all small molecule target classes. Taros Chemical covers the full range of organometallic chemistry research and production from lab scale size to several hundred Kgs supply per year. This includes screening/focused library design and production, computer aided drug design, medicinal chemistry services engaged in hit finding, hit to lead and lead optimization works as well as material science and specialty chemistry driven R&D services including research, design, route scouting, process development and non-GMP production & delivery of up to 1.000kg / year of such performance chemicals. Taros Chemicals have developed TarosGate®, a unique software suite putting cost, time and chemistry information at a Project Leader's finger tips - 24h/7 from anywhere in the world. TarosGate® is a major cornerstone of the 196 Mio. Euro European Lead Factory (ELF) drug discovery platform. Taros Chemicals is leading ELF's chemistry activities since 2013. www.tarosdiscovery.com

About Research Centre Jülich

The increasing level of digitization both requires and enables innovations in the areas of high-performance computing, scientific simulation, and big data, as well as on future technologies such as quantum computing and neuromorphic computing. Jülich scientists also explore the coding of information in molecular-biological structures such as proteins and neural information processing in the human brain. Understanding the complex processes of the brain is crucial to a more effective diagnosis and treatment of brain diseases.

References

1 van Hecke O, Torrance N, Smith BH. Chronic pain epidemiology and its clinical relevance. Br J Anaesth. 2013; 111(1):13-8.

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