

PRESS RELEASE

QSPainRelief - €6.24 million EU-funded research project on improved treatment of chronic pain kicks off

10 European institutions collaborate for the next 5 years to help patients suffering from chronic pain with novel combinational treatments

- *Chronic pain severely reduces the patients' quality of life, their ability to work, and their socio-economic contribution in society. 20% of Europeans suffer from chronic pain, and up to 60% of these patients don't receive effective treatment. It is crucial to help affected individuals.*
- *In the 5-year-long EU-funded QSPainRelief project, world-leading experts on chronic pain, pharmacology, pharmacogenomics, personalised medicine, systems biology, and in silico modelling join forces to develop novel, personalised, and effective combinational treatments of existing medications.*
- *The overarching goal is to identify alternative combinational treatment paradigms, with improved analgesia (pain relief) and reduced adverse effects via a mechanism-based Quantitative Systems Pharmacology (QSP) approach, using algorithms and advanced in silico technologies, and then validate the most promising combinational medication paradigms in preclinical models, in healthy volunteers, and in clinical practice.*

Current treatments of chronic pain largely ineffective

Suffering from chronic pain is both physically and emotionally debilitating. It is extremely hard to focus on daily tasks when being constantly distracted or incapacitated by the pain, while enduring the stigma of having a disease that is not readily obvious on the outside. About 20% of Europeans suffer from chronic pain, and the prevalence of chronic pain is higher in women, compared to men, and increases with age. Only 40% of these patients report adequate pain relief treatment, while 60% of the patients do not experience proper pain relief upon treatment or suffer from confounding adverse effects. The socioeconomic impact is greater than in other health conditions because chronic pain patients are frequently absent from work or have to leave the work force entirely due to their debilitating condition.

Therapy with a single medication is often ineffective and associated with severe adverse effects. For example, the prescription of opioids, which are a frequently used class of pain medications (analgesics) are effective for some, but not all chronic pain patients, and side effects and adverse outcomes include unwanted sedation, cognitive impairment, and the liability of addiction and abuse.

In contrast, so called combinational therapies, meaning for example an opioid in combination with anti-anxiety or anti-depressant medications, or other existing medications that act beneficially on the central nervous system (CNS) are more promising and may lead to an improved and healthier balance of therapeutic benefits versus adverse effects. Novel technologies, such as *in silico* pharmacology (computerised prediction and analysis of distribution and effects of medications in the body),

pharmacogenetics (studying why and how people respond differently to certain medications based upon their individual genetic background), and systems biology (holistic multi-organ, whole-body approaches), nowadays allow for much more personalised therapeutic approaches than in the past. Quantitative Systems Pharmacology (QSP) merges these novel technologies to tailor treatments to the specific needs of individuals and stratified patients groups.

How chronic pain patients will benefit from QSPainRelief

QSPainRelief is an acronym of the full project title and the consortium's goal, namely "*Effective combinational treatment of chronic pain in individual patients by an innovative Quantitative Systems (QSP) Pharmacology pain relief approach*".

In order to reach this goal, QSPainRelief pursues five critical objectives. The first imperative is to develop an *in silico* tool (a computational platform) to identify novel potential combinations of existing medications in a cost-effective manner. The most promising *in silico*-identified combinational treatment paradigms will then be validated in preclinical animal studies and in stratified patient groups, according to each patient's genetic background, personal disease history, and individual needs. The second objective is, of course, to deepen the scientific understanding of the underlying physiological mechanisms of both the pathophysiology of chronic pain as well as the best possible analgesia (pain relief) while reducing side effects to a minimum. The third objective is to better understand the influence of individual differences, such as age, sex and gender, genetic predisposition, causal diseases, and comorbidities regarding the efficacy of analgesic treatments to be able to stratify patients properly and personalise and improve pain treatment for individual patients. The fourth objective is to communicate research results frequently, clearly, and widely to affected individuals, patient organisations, scientists, and the general public, and to develop clinical guidance documents for health care providers, health insurance agencies, policy makers, and regulators. The latter is absolutely crucial to generate real-life impact in improving the quality of life for chronic pain patients. The fifth objective is of direct socioeconomic nature, namely to increase innovative research opportunities. Since four small and medium-sized enterprises (SMEs) are key partners within QSPainRelief, this objective has been already partially met.

Expected impacts of QSPainRelief, creating direct benefits for chronic pain patients, are 1) the development and implementation of novel combinational treatment strategies in clinical practice, 2) a higher treatment efficacy due to personalised medicine and effective patient stratification, 3) improved acceptance of combinational therapies in the clinical setting, and 4) reduced stigmatisation of chronic pain as a health condition through improved and clear communication to and with the general public.

Introducing the QSPainRelief consortium

Professor Dr. Liesbeth de Lange, professor for Predictive Pharmacology in the Division of Systems Biomedicine & Pharmacology at the Leiden Academic Center for Drug Research (LACDR) at Leiden University, The Netherlands, spearheads and coordinates QSPainRelief. The 10 institutions that collaborate in this multi-centre project are spread throughout Europe, and include world-class experts on chronic pain, QSP computational pharmacological modelling, preclinical and clinical research, ethics, science communication, project management, and training of early career scientists in academia, health care, and industry. The multidisciplinary team will ensure high-impact dissemination of scientific results and appropriate implementation in form of clinical guideline development. A major strength of QSPainRelief is that the *in silico* pharmacological modelling will be based on existing medications and published data to identify and validate novel and more effective combinational therapies, and as such the

project avoids the uncertainty of *de novo* R&D and is likely to create real world impact and help chronic pain patients already within the 5-year runtime of the project or shortly thereafter.

The consortium's team leaders will meet in person at least twice a year to discuss the project's progress. The project was successfully kicked off in form of the first general assembly (GA) meeting in Leiden, The Netherlands from January 21nd to 23rd 2020. These are the partners in the QSPainRelief consortium:

- Alma Mater Studiorum – Università di Bologna (UNIBO), Bologna, Italy
- Cliniques universitaires Saint-Luc (CUSL), Bruxelles, Belgium
- concentris research management gmbh (concentris), Fürstenfeldbruck, Germany
- In Silico Biosciences, Inc. (ISB), Lexington, MA, United States
- PD-value B.V. (PD-VALUE), Houten, The Netherlands
- Stichting Centre for Human Drug Research (CHDR), Leiden, The Netherlands
- Universitat Autònoma de Barcelona (UAB), Barcelona, Spain
- Universitat Pompeu Fabra (UPF), Barcelona, Spain
- Université catholique de Louvain (UCL), Louvain-la-Neuve, Belgium
- Universiteit Leiden (ULEI), Leiden, The Netherlands

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