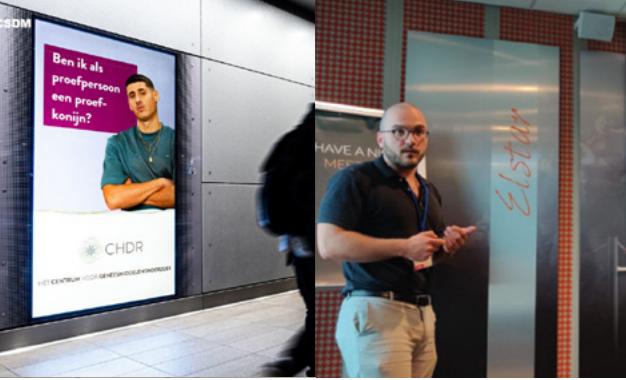


CHDR
Centre for Human Drug Research

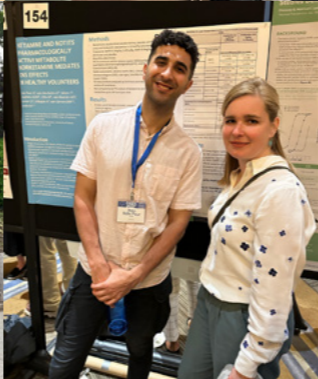
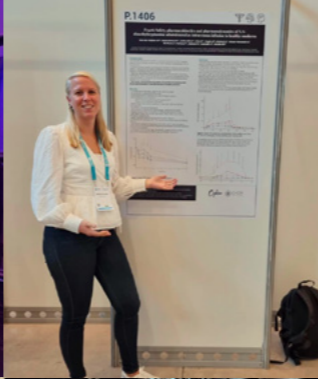
Highlights 2023





Foreword

We proudly present our highlights of 2023. It was a year of growth at CHDR. We conducted a record number of studies, expanded our site facilities and invested in our people. This report provides a glimpse into our upcoming annual report, highlighting key achievements from breakthroughs in drug development to methodological innovations and the ongoing expansion of our team. Join us in celebrating a year of dedication, collaboration and excellence at CHDR.



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2023 in numbers



62

studies conducted

17 patient and 45 healthy volunteer studies



>20,000

volunteer applications

5,000 patients,
15,000 healthy volunteers



43

average days clinical
trial application
approval time



17

clinical trial applications
under the EU CTR

13 approved in 2023, 4 pending



4

clinical pharmacology
graduates



10

legislation and clinical
research certifications



8

PhDs graduated



>90%

studies executed as planned



81

articles published in
peer-reviewed journals



23

contracts signed



+27%

growth in unit occupancy

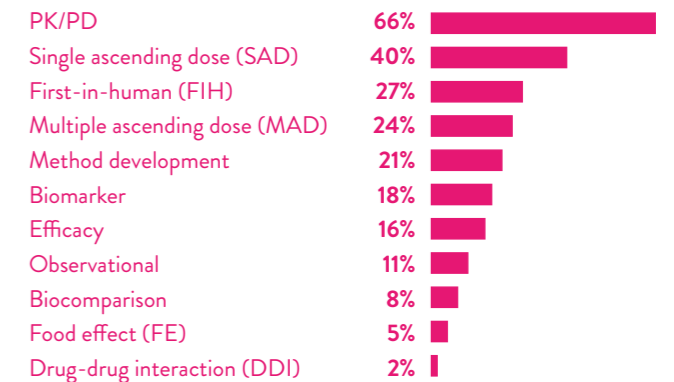


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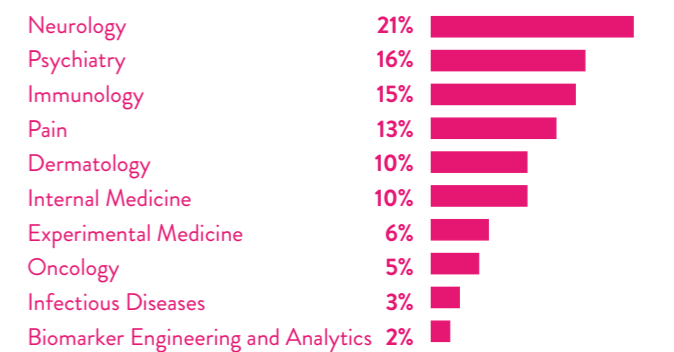
overall client
satisfaction



TYPES OF STUDY



STUDIES PER RESEARCH AREA



CHDR expansion

This year we celebrated the opening of two new research units and our new office space.



September

In September, we opened a new unit in the Leiden University Medical Center (LUMC), adding 8 beds to our research unit, expanding our capabilities and increasing our collaboration with the LUMC.

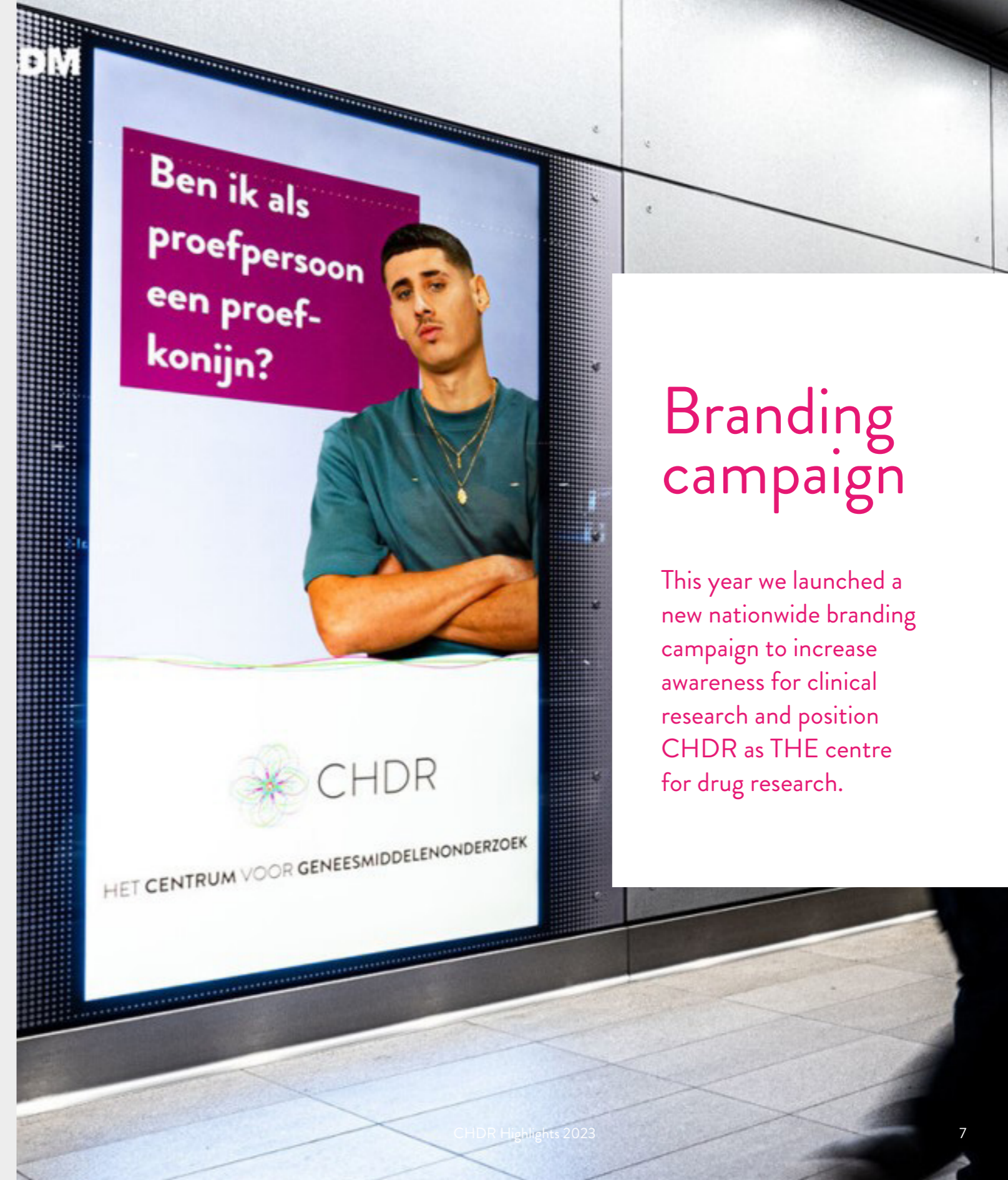
October

In October, we officially opened new office space for support staff in the Leiden Bio Science Park to accommodate our expanding team.



December

In December, we opened brand-new isolation rooms designed to conduct Controlled Human Infection Model (CHIM) studies involving class 2 pathogens.



Branding campaign

This year we launched a new nationwide branding campaign to increase awareness for clinical research and position CHDR as THE centre for drug research.

Dermatology

DERMATOLOGY



Highlights

- First deep phenotyping study conducted at CHDR's LUMC unit.
- Enrolled 43 patients with cutaneous T-cell lymphoma (orphan disease) enrolled in 4 months.
- Discovered novel disease biomarkers and treatment biomarkers for mycosis fungoides.
- Performed full characterisation of epidermal wound model in healthy volunteers and patients with atopic dermatitis.
- Full validation of non-invasive, multimodal imaging pipeline in psoriasis and cutaneous T-cell lymphoma.
- Achieved annual record of more than 700 taken suction blisters and skin punch biopsies (Immunology and Dermatology together).



Collaborations & conferences

- Next Generation ImmunoDermatology: Nationwide, patient-centric consortium celebrates the project launch at Boerhaave Museum Leiden.
- Total of 26 oral and poster abstracts presented in Berlin, Boston, Cambridge, Florence, Glasgow, Kyoto, Montpellier, Tokyo, Utrecht and Vienna.
- Newly established tissue analysis pipeline of skin punch biopsies together with LUMC dept of Dermatology & Pathology (imaging mass cytometry).



Key publications

- Guselkumab induction therapy demonstrates long-lasting efficacy in patients with mild psoriasis, results from a randomized, placebo-controlled exploratory clinical trial. Rousel J, Bergmans ME, van der Meulen LWJ, et al. *J Am Acad Dermatol*. Published online October 5, 2023. DOI: [10.1016/j.jaad.2023.09.071](https://doi.org/10.1016/j.jaad.2023.09.071)
- The vulvar microbiome in lichen sclerosus and high-grade intraepithelial lesions. Pagan L, Huisman BW, van der Wurff M, et al. *Front Microbiol*. 2023;14:1264768. Published 2023 Nov 29. DOI: [10.3389/fmicb.2023.1264768](https://doi.org/10.3389/fmicb.2023.1264768)
- Lesional skin of seborrheic dermatitis patients is characterized by skin barrier dysfunction and correlating alterations in the stratum corneum ceramide composition. Rousel J, Nädäban A, Saghari M, et al. *Exp Dermatol*. Published online November 16, 2023. DOI: [10.1111/exd.14952](https://doi.org/10.1111/exd.14952)
- A multimodal, comprehensive characterization of a cutaneous wound model in healthy volunteers. Ten Voorde W, Saghari M, Boltjes J, et al. *Exp Dermatol*. 2023;32(7):1028-1041. DOI: [10.1111/exd.14808](https://doi.org/10.1111/exd.14808)



Experimental Medicine



Highlights

- Established **Experimental Medicine** as a **new therapeutic area**, studying compounds with target indications in epilepsy, pain and psychiatric disorders.
- Completed **four** clinical studies;
 - All **three** studies with topline results, showed drug activity.
 - **Two** studies used Transcranial Magnetic Stimulation (TMS) as a biomarker for PD effects of investigational compounds.
- **Validated a new method:** Latent Addition - an extension of the Nerve Excitability Threshold Tracking (NETT) technique.
- Performed over **500 TMS-EMG + TMS-EEG measurements** in 2023 in healthy volunteers and patients.



Collaborations & conferences

- Presented our work at the European Conference on Clinical Neurophysiology (ECCN) in Marseille.



This year we performed over 500 TMS-EMG and TMS-EEG measurements for various studies, establishing Experimental Medicine as a new therapeutic area at CHDR.

Infectious Diseases



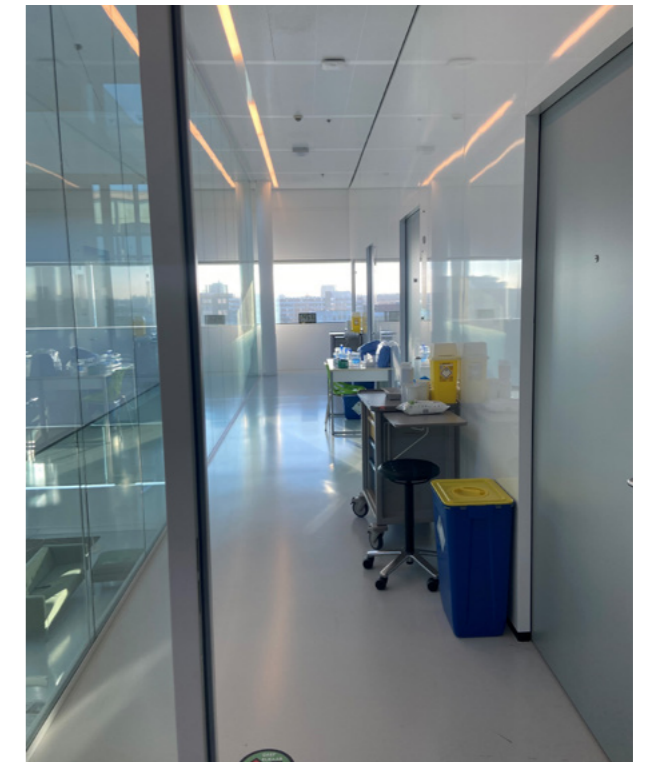
Highlights

- Awarded a research grant from FLUniversal to collaborate on developing a universal influenza vaccine.
- Received ethical approval to set up a rhino challenge model.
- Opened a new isolation unit to conduct Controlled Human Infection Model (CHIM) studies.



Collaborations & conferences

- Three scientific presentations at the European Scientific Working Group on Influenza (ESWI) congress in Valencia.



Our newly opened isolation unit for Controlled Human Infection Model (CHIM) studies is a major step forward. It allows the study of class 2 pathogens in a controlled environment, facilitating pioneering research on therapeutics and vaccines for infectious diseases by safely exposing healthy volunteers to infectious pathogens.



Key publication

Causal chemoprophylactic activity of cabamiquine against *Plasmodium falciparum* in a controlled human malaria infection: a randomised, double-blind, placebo-controlled study in the Netherlands. van der Plas JL, Kuiper VP, Bagchus WM et al. *Lancet Infect Dis.* 2023 Oct;23(10):1164-1174. DOI: [10.1016/S1473-3099\(23\)00212-8](https://doi.org/10.1016/S1473-3099(23)00212-8)



Immunology



Highlights

- Completed highly efficient FIH study for inflammatory diseases: 6 SAD cohorts, 1 MAD cohort, 1 CSF cohort and 1 food interaction cohort in 4.5 months.
- Initiated functional immunomonitoring in autoimmune patients (systemic lupus and rheumatoid arthritis) by in vivo immune challenge models.
- Undertook successful proof-of-mechanism studies for p38 MAPK and IRAK4 inhibitors.
- In vivo immune challenge model development:
 - Refinement of KLH neoantigen challenge (controlled T cell-driven immune response).
 - Development of human complement challenge models.
 - RNA sequencing of imiquimod-induced TLR7-mediated skin inflammation.
 - Development and benchmarking of mucosal immune challenge model.



Collaborations & conferences

- Strategic partnership with big pharma for proof-of-mechanism studies, bridging FIH healthy volunteer studies and phase 1b studies in patients.
- Work presented at national and international conferences: Dutch Society for Immunology (NVVI) in Antwerp, International Congress of Immunology (IUIS) in Cape Town, Complement Summit in Boston, International Societies for Investigative Dermatology (ISID) in Tokyo, European Academy of Dermatology and Venereology (AEDV) in Berlin.



Key publications

Oral prednisolone suppresses skin inflammation in a healthy volunteer imiquimod challenge model. Assil S, Buters TP, Hameeteman PW, et al. *Front Immunol.* 2023;14:1197650. Published 2023 Jul 20. DOI: [10.3389/fimmu.2023.1197650](https://doi.org/10.3389/fimmu.2023.1197650)

Immunosuppression by hydroxychloroquine: mechanistic proof in in vitro experiments but limited systemic activity in a randomized placebo-controlled clinical pharmacology study. In 't Veld AE, Grievink HW, van der Plas JL, et al. *Immunol Res.* 2023;71(4):617-627. DOI: [10.1007/s12026-023-09367-3](https://doi.org/10.1007/s12026-023-09367-3)



Neurology



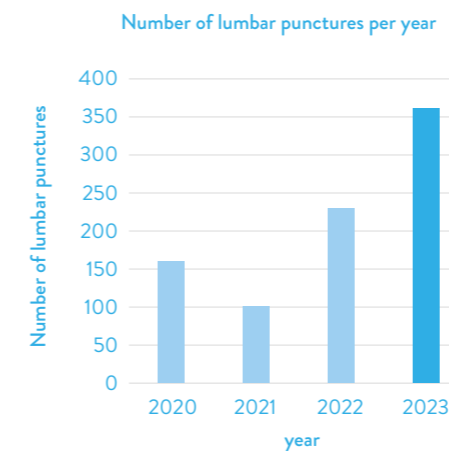
Highlights

- Developed novel method at CHDR for epilepsy studies: **intermittent photic stimulation** in photosensitive epilepsy patients.
- Initiated the **first study in cerebrospinal fluid dynamics**, expanding our neurology capabilities.
- Performed a **record** number of **lumbar punctures**.



Collaborations & conferences

- Collaborated with Haga Hospital for the first time to **expand our patient recruitment capabilities** for studies with cognitive disorders including Alzheimer's disease.
- Poster and/or oral presentation at the Alzheimer's Disease/Parkinson's Disease (AD/PD) conference 2023 in Gothenburg, the Movement Disorder Society (MDS) congress 2023 in Copenhagen and the European Network for the Cure of ALS (ENCALS) meeting in Barcelona.



Key publications

A Phase 1B Trial in GBA1-Associated Parkinson's Disease of BIA-28-6156, a Glucocerebrosidase Activator. den Heijer JM, Kruithof AC, Moerland M et al. *Lansbury P Mov Disord.* 2023 Jul;38(7):1197-1208. DOI: [10.1002/mds.29346](https://doi.org/10.1002/mds.29346)

Smartphone and Wearable Sensors for the Estimation of Facioscapulohumeral Muscular Dystrophy Disease Severity: Cross-sectional Study. Zhuparris A, Maleki G, Koopmans I, et al. *JMIR Form Res.* 2023;7:e41178. Published 2023 Mar 15. DOI: [10.2196/41178](https://doi.org/10.2196/41178)

LRRK2 Inhibition by BIIB122 in Healthy Participants and Patients with Parkinson's Disease. Jennings D, Huntwork-Rodriguez S, Vissers MFJM, et al. *Mov Disord.* 2023;38(3):386-398. DOI: [10.1002/mds.29297](https://doi.org/10.1002/mds.29297)

Pain

PAIN



Highlights

- Demonstrated that **cannabidiol doesn't have any effects on nociceptive thresholds** in humans and doesn't attenuate the psychomimetic or other CNS effects of tetrahydrocannabinol, the most important constituent of cannabis.
- Obtained approval to start with a large clinical study in patients with **neuropathic pain** to elucidate which patients respond to **treatment with cannabis**. In the context of this study **patients will be deeply phenotyped**, which will **establish a cohort of 200 patients** with a broad range of different neuropathic pain syndromes.
- Tested the third **Nav1.8 selective sodium channel blocker using CHDR's trademarked PainCart** test battery in healthy subjects.



Collaborations & conferences

- At the European Pain Federation (EFIC) congress 2023 we hosted a symposium related to the QSPainRelief consortium. We presented the results of a study in which **opioid sparing effects** of pregabalin were **demonstrated using the PainCart** test battery in healthy subjects.



Key publications

Neurocognitive Effect of Biased μ -Opioid Receptor Agonist Oliceridine, a Utility Function Analysis and Comparison with Morphine. Moss L, Hijma H, Demitrack M et al. *Anesthesiology*. 2023 Dec 1;139(6):746-756.
DOI: [10.1097/ALN.0000000000004758](https://doi.org/10.1097/ALN.0000000000004758)

A crossover study evaluating the sex-dependent and sensitizing effects of sleep deprivation using a nociceptive test battery in healthy subjects. Hijma H, Koopmans I, Klaassen E, et al. *Br J Clin Pharmacol*. 2023 Jan;89(1):361-371.
DOI: [10.1111/bcp.15505](https://doi.org/10.1111/bcp.15505)

Psychiatry



Highlights

- Completed CHDR's **first** data-intensive, healthy volunteer study with **intravenously administered dimethyltryptamine (DMT)**.
- Concluded the SAD and food effect parts of CHDR's **first** FIH study with a novel, **non-hallucinogenic psycho/neuroplastogen**.
- Completed two data-intensive SAD/MAD studies with innovative DMT and ketamine analogues.
- Received ethics committee approval for a **Proof of Concept** study in major depressive disorder patients with a novel subtype selective NMDAR antagonist. The approval was based on the PD, PK and safety data gathered in the SAD and MAD conducted at CHDR.
- Characterised 2-AG in plasma and CSF as potential candidate **biomarker** for novel **endocannabinoid MAGL inhibitors**.
- **Achieved technical and clinical validation** of the **Grip Effort Task (GET)** as a potential pharmacological biomarker for reward processing.



Collaborations & conferences

- Presented CHDR's investigator-initiated study **characterising** the PK and PD of **esketamine** and its active metabolite **noresketamine** following IV and PO administration in healthy volunteers at the annual Society of Biological Psychiatry (SOBP) meeting in San Diego.
- Poster presentations on a **validation** study of **intravenous biperiden** as a **pharmacological cognitive challenge model** in healthy elderly volunteers and on a SAD IV infusion DMT study performed at CHDR at the annual ECNP meeting in Barcelona.
- **Presentation and panelist** on psychedelics in early drug development at the Dutch Neuroscience Meeting and the OPEN foundation's DMT event.
- Established a group of trained **psychedelic guiders** in collaboration with the Department of Psychology, Leiden University.



Key publications

Translatability of preclinical to early clinical tolerable and pharmacologically active dose ranges for central nervous system active drugs. Ferreira GS, Dijkstra FM, Veening-Griffioen DH, et al. *Transl Psychiatry*. 2023 Mar 1;13(1):74. DOI: [10.1038/s41398-023-02353-1](https://doi.org/10.1038/s41398-023-02353-1)

Pharmacological characterization of the selective orexin-1 receptor antagonist JNJ-61393215 in healthy volunteers. Brooks S, Zuiker R, Bleys C, et al. *J Psychopharmacol*. 2023;37(6):577-589. DOI: [10.1177/02698811231167989](https://doi.org/10.1177/02698811231167989)

Characterization of the central nervous system penetrant and selective purine P2X7 receptor antagonist JNJ-54175446 in patients with major depressive disorder. Recourt K, de Boer P, van der Ark P, et al. *Transl Psychiatry*. 2023;13(1):266. Published 2023 Jul 24. DOI: [10.1038/s41398-023-02557-5](https://doi.org/10.1038/s41398-023-02557-5)



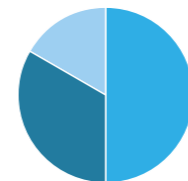
Trial@home



Highlights

- Trial@home was used in a wide variety of trials in 2023.

- Oncology
- Dermatology
- Psychiatry



In these trials, Trial@home was used for exploratory endpoints as well as a convenient follow-up tool increasing the trial output and reducing the burden of clinical trials on participants.

- Machine Learning model developed monitoring depression.
- Demonstrated the use of the Trial@home technology to the wider public during the Leiden International Film Festival by monitoring over 80 filmgoers during 4 movies.



Collaborations & conferences

- Collaborated with the Dutch Cancer Society (KWF) for a pancreatic cancer clinical trial.



Digital equipment used in Trial@home.



Key publications

Trial@home non-invasive home-based assessment of drug effects in early clinical psychiatric drug development: [download \(chdr.nl\)](#)

A smartphone- and wearable-based biomarker for the estimation of unipolar depression severity. Zhuparris A, Maleki G, van Londen L, et al. *Sci Rep.* 2023 Nov 1;13(1):18844. DOI: [10.1038/s41598-023-46075-2](https://doi.org/10.1038/s41598-023-46075-2)

PhD theses

Eight PhD candidates successfully defended their thesis in 2023: Congratulations to Samantha Prins, Bertine Huisman, Willem Birkhoff, Maurits Visser, Johan van der Plas, Wieke Grievink, Lisa Pagan, and Victor Baart.

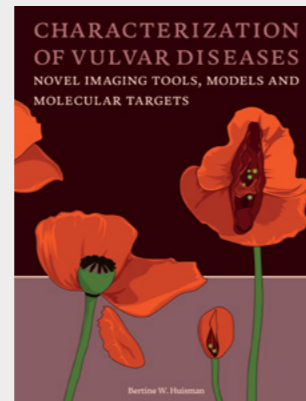
Congratulations!

Find their PhD thesis here: [Library – CHDR](#)



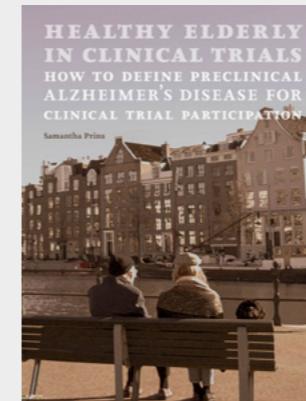
Johan van der Plas

Advances in Clinical development for vaccines therapeutics against respiratory virus infections



Bertine Huisman

Characterization of vulvar diseases



Samantha Prins

Healthy elderly in clinical trials



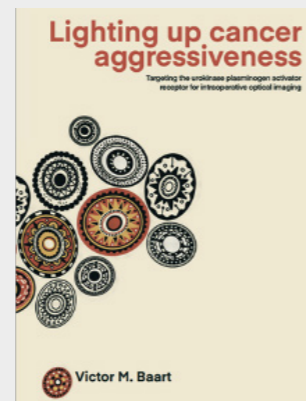
Willem Birkhoff

Measurement of microcirculation in clinical research



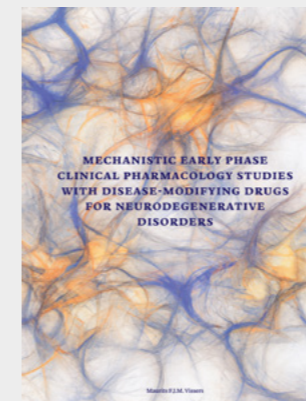
Lisa Pagan

Taking a closer look



Victor Baart

Lighting up cancer aggressiveness



Maurits Visser

Mechanistic early phase clinical pharmacology studies



Wieke Grievink

Immunity in atherosclerosis



C
Vergaderen

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