Deliverable 14

Report on SOP coordination on standardization of animal experiments (M42)

Challenge of reference:

D14 relates to various challenges of reference:

Challenge 1. Existing drugs for human and animal neglected infections against VBD are scarce, with limited efficacy and toxicity. Therefore, a collective effort for innovative compounds and prediction tools should be identified to improve the therapeutic properties of the antiparasitic drugs and identify new drugs.

Challenge 2. The impact of pharmaceutics and their R&D process on the environment is high and it is responsible of huge loss due to contaminated water that affects human and animal health, generate drug resistance problems. Integrated multidisciplinary efforts (design, synthesis/extraction, in vitro and in vivo biological/animal studies, delivery) should be developed to reduce the drugs impact on the environment at every step of the drug research and development process. This requires the coordinated action of researchers and stakeholders (governmental bodies, patients' organizations, industries and SME.

Challenge 3. Not enough control and informed procedures are available to link the environmental impact to drug production and use. Specific guidelines do not exist to address the problem during the whole process from conception to manufacturing and use. Concepts and strategic support in a guideline/white paper format should be given to the stakeholder in the field for a standard approach to develop safer drugs for humans and animals.

Challenge 4. Researchers approaches, industrial entities working in the field of VBD, lack communication and interactions in relation to environmental sustainability and innovation. OneHealthdrugs will represent the ideal platform for networking and communication, to establish interaction and contribute to the training of young researchers.

Objective of reference (Research Coordination Objective)

Objective 3. Coordination of the translation from in vitro-to-in vivo activities to obtain high-quality leads and candidates. Actions: Introduction of omics technologies (genomic, proteomics and transcriptomics) and imaging for a limited number of validated leads. Drug delivery of biodegradable nanotechnology and drug targeting tools applications for both H&A R&D, pharmacology (pharmacokinetics and pharmacodynamics) on animal models by changing drug regimen and study of the effects of the different drug bioavailability tools. This can be acquired through European RTD organization and allow the achievement of high-quality leads with associated biological properties tailored for the H&A VB parasitic infections drug research program. KPI: 3 metrics adopted to measure objective 3 to be reviewed once a year. 3.1 Number of successful examples of biodegradable nanotechnology formulation on dose regimen for each infection. 3.2 Number of projects developed in collaboration with the RTD platform and other stakeholders. 3.3 Number of animal studies including the degradable formulation and targeting vectorization.

Working group of reference:

WG3. Integration of early phase studies and low environmental impact actions.

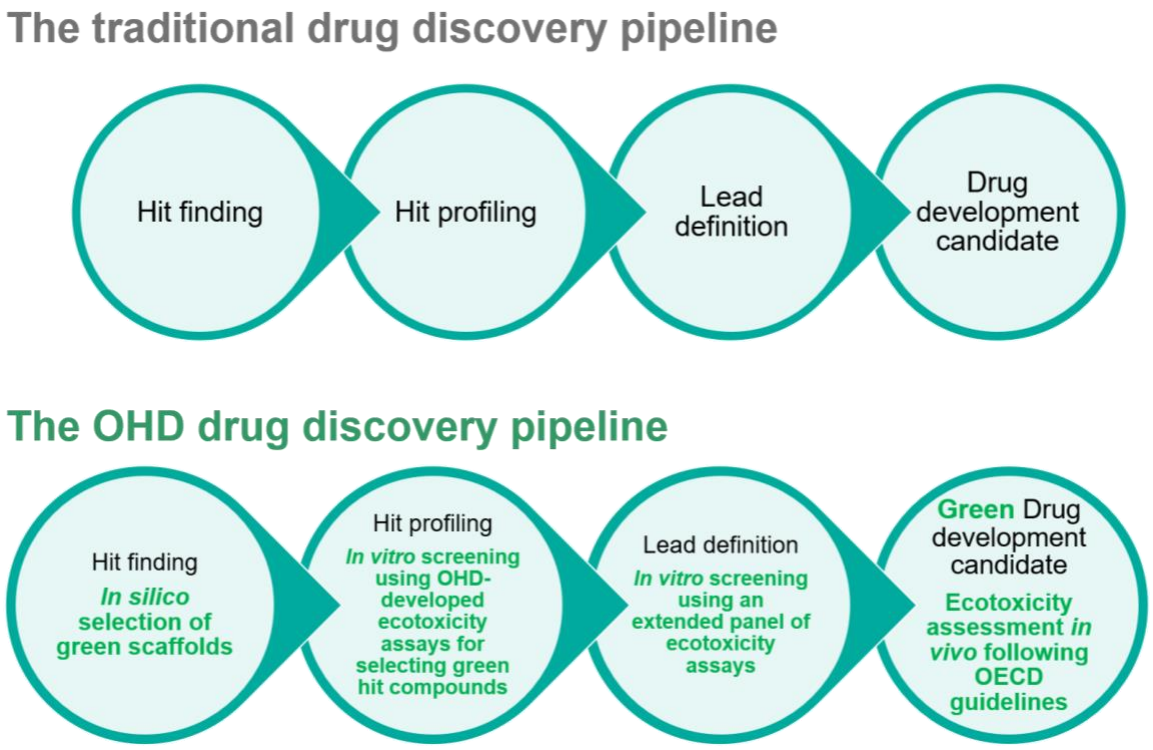
Objectives: Obtain new compounds from different sources and study those compound in vitro for profiling and selection for advances in the process.

T3.4 SOP coordination on standardization of animal experiments through the collaboration with the European RTD platforms and Action platforms. In vivo studies design, use of prediction tools for reducing the number of animals. (D3.4)

Deliverable description.

OHD has presented an updated drug discovery pipeline in which there is a deviation from the standard drug discovery pipeline by inclusion of various green initiatives (Figure). The hit finding is supplemented with new in silico tools for the selection of green scaffolds. In addition, the hit profiling and lead definition phase can rely now on a set of OHD adopted and newly developed ecotoxicity assays. For regulatory approval, additional ecotoxicity testing against aquatic and terrestrial organisms in OECD test protocols remain needed, but the early inclusion of the in silico characterization and ecotoxicity tests will increase the chances of green drug development candidate.

Within the aim to deliver more compelling proof-of-concept read-outs, a trilogy roadmap was published in open access. The raodmap presents a systematic flow-chart of laboratory experiments and decision criteria. Next to precision experimental design and reporting, an overview is provided of various complementary laboratory models. Technical aspects of conventional in vitro and in vivo approaches and, more recently, in silico methods are presented with reference to specific preclinical R&D stages to support a more focused early development path that remains accessible to engaged stakeholders.



Following activities were organized to support the coordination on standardization of animal experiments, focussing on 4 intertwined themes (i) Animal and alternative models, (ii) on- and off-target predictions, (iii) formulation and (iv) environmental impact regulations and impact assessment.

Animal and alternative models

A series of workshops, a training school and a conference was organized to cover several aspects of preclinical research in cell cultures and animal models, including principles of 3R and reporting according to the ARRIVE guidelines. As part of the refinement and reduction of animal research, several new imaging technologies have found their introduction in drug discovery for infectious diseases. Also, the limitations of animal models and a broader perspective beyond mouse models is offered. The training school focused on in vitro examinations of the antiparasitic activity and toxic effects on selected cell lines. The study of the drug's toxicity should also consider that the drug will be released into the environment. Therefore, evaluating its toxicity towards representative organisms in the ecosystem is essential. The conference served as a platform to present and discuss the OHD green drug discovery roadmap.

- WG3 Workshop 2 “Animal models for lead selection against vector borne parasitic diseases within one Health concept” 8 September 2023 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2023/animal-models-for-lead-selection-against-vector-borne-parasitic-diseases-within-the-one-health-concept/

- WG3, WG4, WG6, HG4, HG5 Thematic Workshop “Animal friendly and environmentally relevant systems to replace or refine animal tests during drug developmental processes for VBD” I3S, Porto, Portugal, 14-15 May 2024

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/environmentally-friendly-systems-to-replace-classical-animal-models-in-drug-testing-for-vbd/

- 2nd Training School "Cell culture as in vitro models for newly developed drugs against vector borne parasitic diseases within the One Health perspective". Warsaw, Poland, 25-27 September 2024.

  https://www.onehealthdrugs.com/events/training-schools/training-school-cell-culture-as-in-vitro-models-for-newly-developed-drugs-against-vector-borne-parasitic-diseases-within-the-one-health-concept/

- OHD 2025 Conference "Strategies for breaking the chain between the parasite reservoir in animals and infections in humans". Antwerp, Belgium, 4-6 June 2025

  https://www.onehealthdrugs.com/events/scientific-meeting/next-meeting/ohd-2025-annual-conference-strategies-for-breaking-the-chain-between-the-parasite-reservoir-in-animals-and-infections-in-humans/

On- and off-target predictions

Several activities were focused on innovative models (in silico and experimental) at the interface of drug discovery for VBDs and (eco)toxicology including biodegradability. This is aimed at not only determining safety for the patient by selectively targeting the pathogen (on-target) but also preventing toxicity to the patient and the environment (off-target). These are becoming integral part of the roadmap and hence impact the in vitro-to-in vivo translation towards a green drug development candidate. The training school covered key aspects such as predictive toxicology models, bioaccumulation forecasting, and the integration of in silico methods into environmental protection strategies.

- WG1, WG2, HG7 Thematic Workshop: "Novel leads and drugs for vector borne diseases: Targets and off targets (toxicity and ecotoxicity) and mechanism of action" Athens, Greece, 19-20 September 2024

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/international-workshop-novel-leads-and-drugs-for-vector-borne-diseases-targets-and-off-targets-toxicity-and-ecotoxicity-and-mechanism-of-action-19-20-09-2024/

- WG4 Workshop "Adverse outcome pathways at early stages of the design of antiparasitic drugs " 17 October 2024 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2023/adverse-outcome-pathways-at-early-stages-of-the-design-of-antiparasitic-drugs-17th-october-2024-9-00-am-4-30-pm-cet-virtual/

- WG2, HG6, HG7 Training School "In silico prediction method for ecotoxicity and bioaccumulation" Attica, Greece, 19-21 March 2025

  https://www.onehealthdrugs.com/events/training-schools/5th-ohd-training-school-in-silico-prediction-method-for-ecotoxicity-and-bioaccumulation/

- WG1, WG2, WG3, HG7 Workshop "In silico and in vitro approaches to assess biodegradability and prioritize environmentally friendly chemotypes" 27 March 2026 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/workshop-online-in-silico-and-in-vitro-approaches-to-assess-biodegradability-and-prioritize-environmentally-friendly-chemotypes-of-synthetic-and-natural-origin/

- WG1-WG6 + all HGs Joint meeting Drug Design & Development Seminar (DDDS) of the German Society for Parasitology (DGP) &The European Cost Action – CA21111 – "OneHealthDrugs" "Human and Animal Parasitic Diseases – Bridging the Innovation Gap – " Giessen, Germany, 17-20 March 2026

  https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/joint-meeting-of-the-26th-drug-design-development-seminar-ddds-2026-of-the-german-society-for-parasitology-dgp-the-european-cost-action-ca21111-onehealthdrugs/

Formulation

In the pursuit of environmentally conscious antiparasitic drug discovery, formulation, nanotechnology and other cutting-edge approaches can impact the in vitro-to-in vivo translation, improve efficacy and selectivity and prevent off-target effects in the environment. Several workshops were organized to address the concepts that can be used.

- WG2, HG7 Workshop "Green chemistry approaches and innovative drug delivery systems towards reducing environmental impact in antiparasitic drug discovery" 15 March 2024 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/green-chemistry-approaches-and-innovative-drug-delivery-systems-towards-reducing-environmental-impact-in-antiparasitic-drug-discovery/

- WG3 Workshop "Formulation technologies for human and veterinary VBDs to reduce dose and environmental impact " 13th September 2024 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/formulation-technologies-for-human-and-veterinary-vbds-to-reduce-dose-and-environmental-impact/

Environmental impact regulations and impact assessment

There are several regulatory aspects that should be analyzed under the One Health framework for an effective multidisciplinary collaboration, targeting sustainability of drug development, its production and distribution. Therefore, to meet the One Health approach expectations for drug development against PVBDs, careful consideration of regulatory aspects that encompass human and animal health, ethical concerns, environmental impact, and international collaboration must be considered. Effective communication and coordination of the early preclinical discovery roadmap is essential to bring safe and effective drugs to both humans and animals.

- WG6 Workshop "Regulatory Issues Associated with drug development for Parasitic Vector-Borne Diseases". 12 October 2023 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2023/regulatory-aspects-of-drug-development-in-europe/

- WG3 Workshop "Antiparasitic veterinary drugs: From the bench to the market crossing (carefully) the environment". 12 December 2024 (VIRTUAL)

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/antiparasitic-veterinary-drugs-from-the-bench-to-the-market-crossing-carefully-the-environment/

- WG4 Workshop "Biomarkers, screening, standardized and non-standardized ecotoxicological testing in One Health drug discovery and development". Giessen, Germany, 20-21 September 2023

  https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2023/biomarkers-screening-standardized-and-non-standardized-ecotoxicological-testing-in-drug-discovery-and-development/

- WG6 Workshop "Principles of veterinary drug development for PVBD, including regulatory aspects, under OneHealth framework". 11 November 2025 (VIRTUAL)

STSM

STSM - Development of NMT-A004-loaded biodegradable nanocarriers - Theano Fotopoulou - 01/06/2024 End date 07/07/2024 / Host Institution - Universidade do Minho, Centro de Física das Universidades do Minho e Porto (CF-UM-UP), Campus de Gualtar, Escola de Ciências, Home Institution Ethniko Idryma Erevnon (Athina, Greece) Athina – Greece

STSM start and end date: 01/06/2024 to 07/07/2024

Working Group: WG2 "Integration of early phase studies and low environmental impact actions" and WG3 "Coordination of the translation from in vitro-to-in vivo activities to obtain One Health high-quality leads and candidates".

Purposes of the STSM

NMT-A004 (Fig.1), an alkyl phosphocholine-dinitroaniline hybrid synthesized by Calogeropoulou's group, despite its broad spectrum antiparasitic activity against Leishmania, T. brucei and T. cruzi Y strain epimastigotes, intracellular amastigotes and trypomastigotes, its SNAP-PK evaluation showed reduced oral bioavailability. As a result, nanoformulation studies were proposed to increase its half-life.

The main purpose of this STSM was the development and characterization of biodegradable nanostructured vectors that improve the pharmacokinetic properties of the lead compound NMT-A004, allowing for sustained delivery. Therefore, in the context of this STSM our aim was to evaluate different types of nanocarriers in terms of their encapsulation efficiency, drug loading content and colloidal stability. The overarching goal of the STSM was to contribute to my career development and broadening of my skillset and knowledge by gaining experience in nanoformulation strategies through the exposure to cutting-edge methodologies and the hands-on experience in the use of state-of-the-art infrastructure available at CF-UM-UP such as Dynamic/Electrophoretic Light Scattering (DLS/ELS) and UV-Vis Derivative Spectroscopy.
Finally, this STSM was a good opportunity to promote the collaboration and transfer of knowledge between Calogeropoulou's group with emphasis on medicinal chemistry towards new drugs for Neglected infectious diseases and Lúcio's group with emphasis on nanotherapeutics and biophysical techniques. The work performed was positive and still ongoing.

STSM - Blood brain barrier – derived peptide shuttles for drug delivery to the CNS - Paula Schwartz - 13/01/2025 24/01/2025 - From Medical University of Vienna (Vienna, Austria) Vienna - Austria to Uppsala Universitet, Department of Pharmacy, Translational PKPD.
The objective of this STSM project was to perform an in vivo infusion study to determine the extent of transport to the brain of a previously designed, synthesized and in vitro screened cyclic peptide. During this STSM project rats were used as model organism and the peptide was administered for four hours to reach steady state conditions. Terminal plasma and brain samples were taken for LC-MS analysis, which will be performed at the home institution. After quantification of the peptide, the partition coefficient to the brain (Kp,brain) will be calculated, which is necessary for the calculation of Kp,uu,brain (unbound brain-to-plasma concentration ratio coefficient). If transport is observed in vivo, the peptide will be further developed and tested as a shuttle for transporting compounds into the brain or to be used as a tool to study therapeutic applications like leishmania infiltrating the CNS.

Publications demonstrating the activities of OHD in the context of D15

Several manuscripts co-authored by multiple OHD members include opinion papers for the inclusion of environmental toxicity testing (in silico and experimental) in the early discovery pipeline, proposals of improved roadmaps, successful in vivo proof-of-concepts for antiparasitic compounds and novel fundamental insights in the in vivo virulence and treatment of parasitic diseases.

<u>Papers advocating for improved drug discovery pipelines:</u>

Cordeiro da Silva A, Calogeropoulou T, Costi MP, Alunda JM. Drugs for Vector-Borne Protozoal Diseases in a One Health Scenario. A European Perspective. ACS Infect Dis. 2024 Nov 8;10(11):3715-3720. doi: 10.1021/acsinfecdis.4c00339. Epub 2024 Oct 29. PMID: 39471826; PMCID: PMC11555669.

Costi MP, Cordeiro da Silva A. One Health and Vector-Borne Parasitic Diseases Virtual Special Issue. ACS Infect Dis. 2024 Dec 13;10(12):4010-4011. doi:10.1021/acsinfecdis.4c00778. Epub 2024 Oct 29. PMID: 39470576.

Ilbeigi K, Barata C, Barbosa J, Bertram MG, Caljon G, Costi MP, Kroll A, Margiotta-Casaluci L, Thoré ESJ, Bundschuh M. Assessing Environmental Risks during the Drug Development Process for Parasitic Vector-Borne Diseases: A Critical Reflection. ACS Infect Dis. 2024 Apr 12;10(4):1026-1033. doi:10.1021/acsinfecdis.4c00131. Epub 2024 Mar 27. PMID: 38533709; PMCID:PMC11019539.

Lima CM, Uliassi E, Thoré ESJ, Bertram MG, Cardoso L, Cordeiro da Silva A, Costi MP, de Koning HP. Environmental impacts of drugs against parasitic vector-borne diseases and the need to integrate sustainability into their development and use. Open Res Eur. 2024 Nov 4;4:207. doi: 10.12688/openreseurope.18008.2. PMID: 39534878; PMCID: PMC11555358.

Hendrickx S, Ilbeigi K, Thoré ESJ, Bertram MG, Calvo-Alvarez E, Cintesun S, Olías-Molero AI, Corral MJ, Mateo-Barrientos M, Estaquier J, Pomel S, Alunda JM, Gul S, Van Bocxlaer K, Frézard F, Tavares J, Da Silva AC, Costi MP, Maes L, Caljon G. A strategic discovery roadmap towards high-quality leads and drug development candidates for kinetoplastid diseases. Part 1: setting the stage. J Antimicrob Chemother. 2026 Apr 3;81(5):dkag109. doi: 10.1093/jac/dkag109. PMID:42085493; PMCID: PMC13142250.

Hendrickx S, Ilbeigi K, Thoré ESJ, Bertram MG, Calvo-Alvarez E, Cintesun S, Olías-Molero AI, Corral MJ, Mateo-Barrientos M, Estaquier J, Pomel S, Alunda JM, Gul S, Van Bocxlaer K, Frézard F, Tavares J, Cordeiro Da Silva A, Costi MP, Maes L, Caljon G. A strategic discovery roadmap towards high-quality leads and drug development candidates for kinetoplastid diseases. Part 2: from molecule to confirmed hit. J Antimicrob Chemother. 2026 Mar 4;81(4):dkag110. doi: 10.1093/jac/dkag110. PMID: 41913953; PMCID: PMC13036319.

Hendrickx S, Ilbeigi K, Thoré ESJ, Bertram MG, Calvo-Alvarez E, Cintesun S, Olías-Molero AI, Corral MJ, Mateo-Barrientos M, Estaquier J, Pomel S, Alunda JM, Gul S, Van Bocxlaer K, Frézard F, Tavares J, Cordeiro Da Silva A, Costi MP, Maes L, Caljon G. A strategic discovery roadmap towards high-quality leads and drug development candidates for kinetoplastid diseases. Part 3: from lead towards a drug development candidate. J Antimicrob Chemother. 2026 May 5;81(6):dkag111. doi: 10.1093/jac/dkag111. PMID: 42108536; PMCID: PMC13158017.

Papers presenting refined in vivo models for drug testing:

Hendrickx S, Feijens PB, Escudié F, Chatelain E, Maes L, Caljon G. In Vivo Bioluminescence Imaging Reveals Differences in Leishmania Infantum Parasite Killing Kinetics by Antileishmanial Reference Drugs. ACS Infect Dis. 2024 Jun 14;10(6):2101-2107. doi: 10.1021/acsinfecdis.4c00109. Epub 2024 May 11. PMID: 38733389; PMCID: PMC11423396.

Hendrickx S, Bulté D, Mabille D, Mols R, Claes M, Ilbeigi K, Ahmad R, Dirkx L, Van Acker SI, Caljon G. Comparison of Bioluminescent Substrates in Natural Infection Models of Neglected Parasitic Diseases. Int J Mol Sci. 2022 Dec 16;23(24):16074. doi: 10.3390/ijms232416074. PMID: 36555716; PMCID: PMC9781651.

Papers demonstrating in vivo potency and safety of antiparasitic molecules:

Van de Velde E, Van Hauwermeiren A, Karalic I, Van Pelt N, Matheeussen A, Feijens PB, Hendrickx S, da Gama Jaén Batista D, de Almeida Fiuza LF, do Carmo CF, Girão RD, Cranshoff Y, De Baere S, Croubels S, Soeiro MNC, Caljon G, Van Calenbergh S. Late-Stage Diversification of Rewired Purine C-Nucleosides Reveals Potent Antitrypanosomatid Agents with In Vivo Efficacy. J Med Chem. 2026 Aug 27;69(16):19744-19758. doi: 10.1021/acs.jmedchem.6c01077. PMID: 42679146.

Santos TT, Lages EB, Ricotta TNQ, de Oliveira LG, Ramos GS, Burlot J, Abreu S, Chaminade P, Legrand FX, Tran P, Deloménie C, Vallejos VMR, Helou DG, de Almeida RM, Queiroz-Junior CM, Teobaldo GBM, de Oliveira CLP, Ferreira LAM, Aguiar MMG, Pomel S, Frézard F. Long-Circulating Liposomes Codelivering Amphotericin B and Retinoic Acid for Cutaneous Leishmaniasis Treatment. ACS Omega. 2025 Oct 7;10(41):48514-48530. doi: 10.1021/acsomega.5c06156. PMID:41141727; PMCID: PMC12547526.

Martinengo B, Baldassarri C, Ilbeigi K, Alkhalaf HE, Sarode A, Elmahallawy EK, Kwon BR, Agyei AS, Abdimanova A, de Almeida Fiuza LF, Azevedo R, da Conceição K, Meuser Batista M, Borges EN, Freitas E Silva KS, Cardoso ÉJS, Monteiro NC, Nunes Lemes LF, Soares Romeiro LA, Alonso A, Soeiro MNC, Caljon G, Brooks BW, De Koning HP, Bolognesi ML. Sustainable

Antiparasitic Agents from an Agro-Industrial Waste: Mitochondria-Targeting Cashew Nutshell Liquid-Derived Phosphonium and Ammonium Salts. J Med Chem. 2025 Sep 25;68(18):19438-19462. doi: 10.1021/acs.jmedchem.5c01617. Epub 2025 Sep 8. PMID: 40920168; PMCID: PMC12481484.

Hrčková G, Mudroňová D, Reiterová K, Cavallero S, Bellini I. Human Dialyzable Leukocyte Extract Enhances Albendazole Efficacy and Promotes Th1/Th2-Biased Lymphocyte and Antibody Responses in Peritoneal Cavity of Murine Model of Mesocestoides vogae Infection. Int J Mol Sci. 2025 Jul 21;26(14):6994. doi: 10.3390/ijms26146994. PMID: 40725240; PMCID: PMC12295987.

Roignant M, Richard J, Donzel M, Rottmann M, Mäser P, Davioud-Charvet E. Design, Synthesis and Antiplasmodial Activities of a Library of Fluorine-Based 3-Benzylmenadiones. Molecules. 2025 Jun 3;30(11):2446. doi:10.3390/molecules30112446. PMID: 40509333; PMCID: PMC12156041.

Ilbeigi K, Mabille D, Roy R, Bundschuh M, Van de Velde E, Hulpia F, Van Calenbergh S, Caljon G. 3'-deoxytubercidin: A potent therapeutic candidate for the treatment of Surra and Dourine. Int J Parasitol Drugs Drug Resist. 2025 Apr;27:100580. doi: 10.1016/j.ijpddr.2025.100580. Epub 2025 Jan 10. PMID:39827514; PMCID: PMC11787584.

Ilbeigi K, Mabille D, Matheeussen A, Hendrickx R, Claes M, Van Reet N, Anthonissen R, Hulpia F, Lin C, Maes L, Regnault C, Whitfield P, Roy R, Ungogo MA, Sterckx YG, De Winter H, Mertens B, Bundschuh M, De Koning HP, Van Calenbergh S, Caljon G. Discovery and Development of an Advanced Lead for the Treatment of African Trypanosomiasis. ACS Infect Dis. 2025 Jan 10;11(1):131-143. doi: 10.1021/acsinfecdis.4c00472. Epub 2024 Dec 12. PMID: 39665421.

Davie T, Serrat X, Imhof L, Snider J, Štagljar I, Keiser J, Hirano H, Watanabe N, Osada H, Fraser AG. Identification of a family of species-selective complex I inhibitors as potential anthelmintics. Nat Commun. 2024 May 8;15(1):3367. doi: 10.1038/s41467-024-47331-3. PMID: 38719808; PMCID: PMC11079024.

Papers revealing new in vivo fundamental insights:

Picard M, Boutrais S, Rodrigues V, Fortier Y, Borde C, Soundaramourty C, Clain J, Joly-Beauparlant C, Racine G, Zghidi-Abouzid O, Droit A, Pruvost A, Costi MP, Silvestre R, Cordeiro da Silva A, MacDougall J, André S, Estaquier J. Persistent myeloid cell reprogramming despite miltefosine treatment in Leishmania-infected macaques. iScience. 2025 Nov 3;28(12):113900. doi: 10.1016/j.isci.2025.113900. PMID: 41321641; PMCID: PMC12663736.

Stijlemans B, De Baetselier P, Van Molle I, Lecordier L, Hendrickx E, Romão E, Vincke C, Baetens W, Schoonooghe S, Hassanzadeh-Ghassabeh G, Korf H, Wallays M, Pinto Torres JE, Perez-Morga D, Brys L, Campetella O, Leguizamón MS, Claes M, Hendrickx S, Mabille D, Caljon G, Remaut H, Roelants K, Magez S, Van Ginderachter JA, De Trez C. Q586B2 is a crucial virulence factor during the early stages of Trypanosoma brucei infection that is conserved amongst trypanosomatids. Nat Commun. 2024 Feb 27;15(1):1779. doi: 10.1038/s41467-024-46067-4. PMID: 38413606; PMCID: PMC10899635.

Dirkx L, Loyens M, Van Acker SI, Bulté D, Claes M, Radwanska M, Magez S, Caljon G. Effect of Leishmania infantum infection on B cell lymphopoiesis and memory in the bone marrow and spleen. FASEB J. 2024 Aug 31;38(16):e23893. doi: 10.1096/fj.202400715R. PMID: 39177943.

Dirkx L, Van Acker SI, Nicolaes Y, Cunha JLR, Ahmad R, Hendrickx R, Caljon B, Imamura H, Ebo DG, Jeffares DC, Sterckx YG, Maes L, Hendrickx S, Caljon G. Long-term hematopoietic stem cells trigger quiescence in Leishmania parasites. PLoS Pathog. 2024 Apr 24;20(4):e1012181. doi: 10.1371/journal.ppat.1012181. PMID: 38656959; PMCID: PMC11073788.

Dirkx L, Hendrickx S, Merlot M, Bulté D, Starick M, Elst J, Bafica A, Ebo DG, Maes L, Van Weyenbergh J, Caljon G. Long-term hematopoietic stem cells as a parasite niche during treatment failure in visceral leishmaniasis. Commun Biol. 2022 Jun 25;5(1):626. doi: 10.1038/s42003-022-03591-7. PMID: 35752645; PMCID:PMC9233693.

Patents:

PCT Patent application (PCT/IB2025/053701) (8/4/2025) -Theodora Calogeropoulou/Anabela Cordeiro da Silva. Putative drug against Leishmaniasis and/or Trypanosomiasis.

Patents on antitrypanosomal nucleoside analogues (PCT/EP2022/077048) – Serge Van Calenbergh, Guy Caljon. Nucleoside analogues for the treatment of parasitic infections.

Pomel S., Frézard F., Chaminade P., Abreu S., Santos T.T., Aguiar M.M.G, Lages E.B., Ricotta T.N.Q., Oliveira L.G. and Vallejos V.M.R. New liposome composition for leishmaniasis treatment. European patent EP25305594.1 deposited by CNRS and Université Paris-Saclay, 25th april 2025. International patent PCT/EP2026/061909 deposited by CNRS and Université Paris-Saclay, 24th april 2026

Interested stakeholders

Experts in medicinal chemistry, parasitology, and environmental toxicology who focus on drug discovery. Computational chemists and biologists involved in in silico prediction modeling. Organizations seeking innovative antiparasitic compounds for drug development pipelines. Stakeholders in pharmaceutical R&D emphasizing environmentally sustainable practices. Agencies interested in setting standards and policies for sustainable drug development with low environmental impact. Researchers participating in “OneHealthdrugs” initiatives or similar global programs aiming at interdisciplinary solutions for health challenges.

Scientific impact (from the MoU)

- Relevant scientific training for Young Researchers and Innovators in a multidisciplinary context favouring their career development
- Discovery and optimization of antiparasitic hits and lead compounds for H&A use with expected environmental low impact and higher quality profile than before
- Ecotoxicology-based model organism selection for biomarkers and indicators assay

The long-term benefits (from the MoU)

- Substantial improvements of the biological profile in treating parasitic diseases caused by VB parasitic diseases affecting humans and animals
- Substantial increase of the One Health awareness in Young Researchers and Innovators and all participants working together on drug discovery and environmental health
- A long-lasting impact on antiparasitic drug development in Europe due to targeted training of Young Researchers and Innovators

- A permanent on-line network of stakeholders in antiparasitic drug discovery and development to maintain a transfer of knowledge, new One Health knowledge creation and strengthen collaboration and engagement of RTD platforms active in the field
- Increased funding into antiparasitic drug development integrated with environmental scientists due to the improved multidisciplinary and multi-centre applications resulting from collaborations between participants in the Action and successful activity of contact and networking within this Action.

Innovation

- IP on new advanced candidates with promising or relevant pharmacological activity
- Implementation of existing and new assays in the discovery roadmap