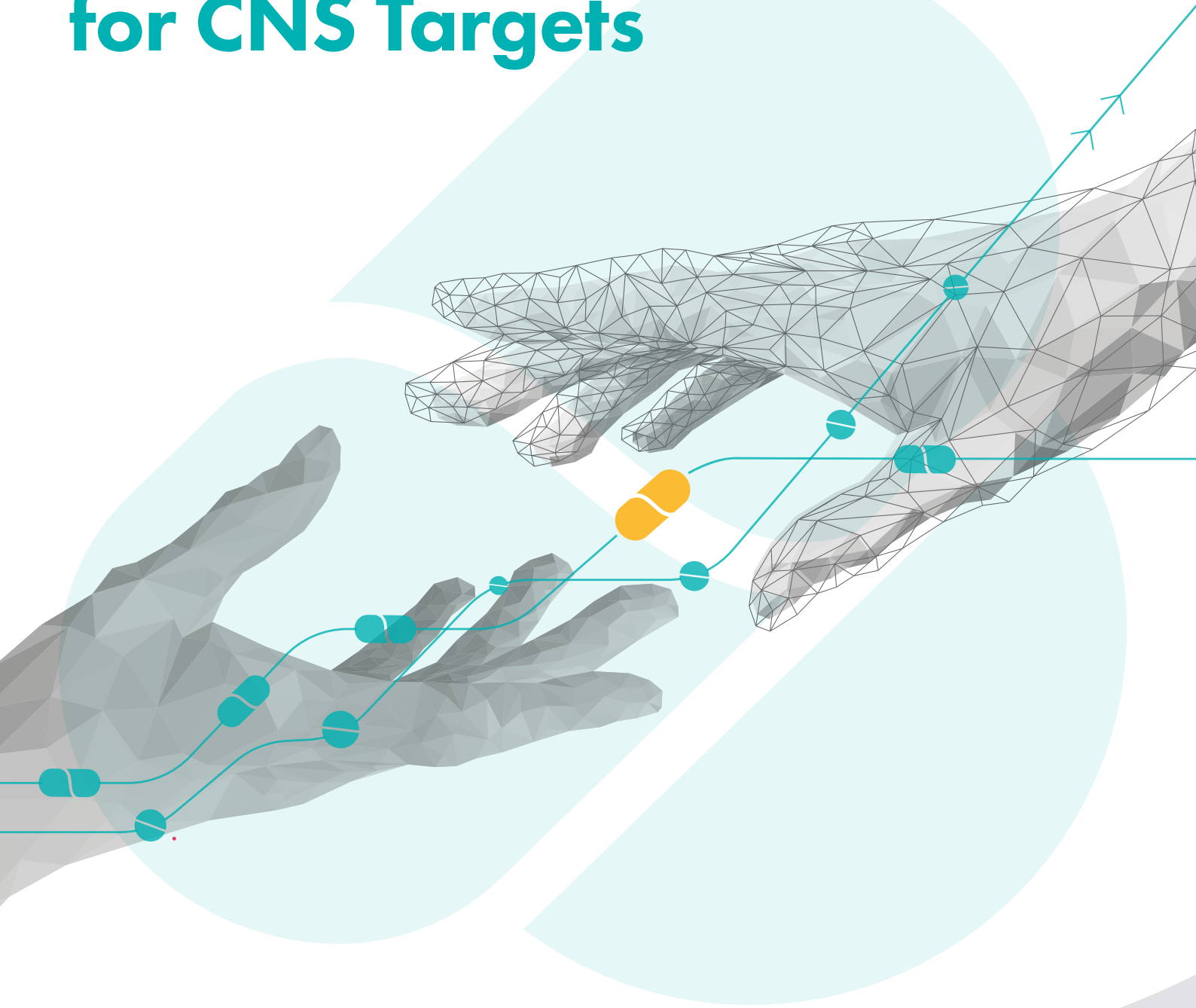


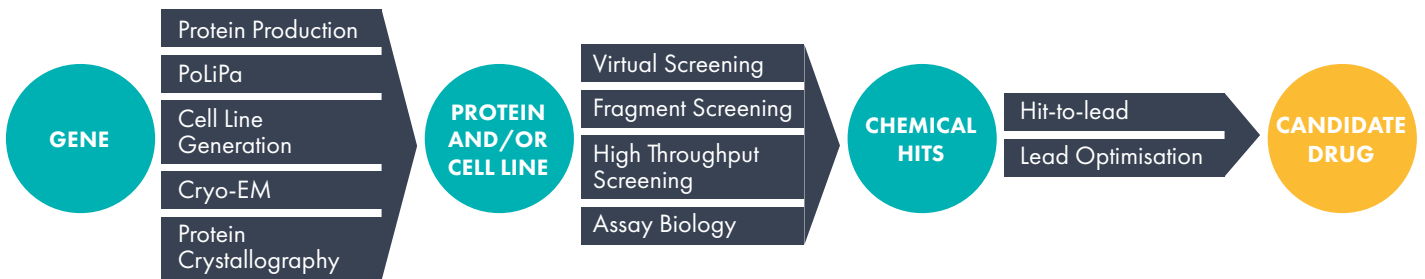
Integrated Drug Discovery for CNS Targets



Integrated CNS Drug Discovery

Our highly experienced interdisciplinary team provides the full range of pre-clinical drug discovery services supporting your **Central Nervous System (CNS)** projects at every stage of the drug discovery journey, from disease target nomination to candidate drug selection, and from protein production, cell line generation and assay development through to medicinal chemistry for lead optimisation.

Our dedicated experts will work collaboratively with you and your team to provide tailored scientific solutions, adding significant value to your drug discovery projects. Our integrated approach has a proven record of success in delivering timely and cost effective solutions and generating new intellectual property for our clients.



Together, with our partners we bring a highly experienced interdisciplinary team, comprising of experts in the following areas and all based locally to Cambridge, UK:

- **Protein expression**
 - o Traditional detergent-based methods
 - o PoLiPa: Domainex's proprietary platform for the efficient preparation of stable and highly purified membrane proteins, without the need for thermostabilising mutations or detergents
- **Structural biology**
 - o Protein crystallography
 - o Cryogenic electron microscopy (cryo-EM)
- **Translational biology**
 - o Biochemical
 - o Biophysics
 - o Cell Biology
 - o Neuroinflammation, chemotaxis and microglial phagocytosis assays
- **Ion channel biology**
 - o Manual and automated patch clamp
 - o Cell-based assays using FLIPR platform
 - o Microelectrode arrays (MEA)
 - o Native and engineered ion channel cell lines, iPSC neurons, trigeminal neurons, rodent dorsal root ganglion (DRG) sensory neurons
- **Hit finding**
 - o High throughput screening (HTS)
 - o Virtual screening
 - o *FragmentBuilder*: Fragment screening (including covalent fragments)
- **Hit-to-lead and lead optimisation medicinal chemistry**
 - o Computer aided drug design
 - o ADME and DMPK (including brain PK)
 - o Blood-brain barrier (BBB) permeability
 - o Animal models
 - o Cardiac safety screening
 - o GLP Toxicology
 - o GLP/GCP Bioanalysis

Our team will successfully guide your drug discovery projects, advancing them from hit identification, hit validation, hit-to lead, lead optimisation to candidate nomination. Making sure the projects are focused, de-risked and kept on track by constantly reviewing project milestones and progression against target product profiles.

Benefits of working with us

- Access to Domainex's expertise in CNS drug discovery including hit-to-lead and lead optimisation medicinal chemistry and structural biology
- Domainex's proprietary PoliPa technology providing access to membrane proteins (<https://www.domainex.co.uk/services/innovative-polymer-lipid-particle-polipa-technology>)
- Access to Pharmidex's expertise in CNS drug discovery and brain DMPK
- Access to Metrion's expertise in ion channel and neuroscience biology
- Access to Cresset Discovery's expertise in computational chemistry methods for CNS drug discovery
- Access to CNS, stroke, pain and behavioural *in vivo* models, including *in vivo* neurotransmitter profiling, established at Pharmidex
- Closely located facilities reducing design-make-test cycles
- Regular alliance meetings held to ensure effective communication
- Metrion's state-of-the-art ion channel drug discovery laboratories with specialist equipment

PARKINSON'S^{UK}
CHANGE ATTITUDES.
FIND A CURE.
JOIN US.

Domainex currently has a major collaboration with **Parkinson's UK**, the largest charitable funder of Parkinson's research in Europe. The collaboration is focused on developing small molecule therapies targeting neuroinflammation that could slow the progression of Parkinson's disease. Inflammation is vital for defending the body from infections, injuries and toxins. However, in Parkinson's there is excessive chronic inflammation within the brain. It is now believed that this may play a role in the damage to brain cells which occurs in the condition. Domainex is conducting an integrated drug discovery programme in order to optimise the pharmaceutical properties within the chemical series with the ultimate aim of nominating a clinical candidate. The goal is to develop a therapy with the potential to slow or stop the progression of Parkinson's, something no current medication can do.

"Domainex was selected following an extensive review process on the basis of their experience and capability to execute a fully integrated drug discovery project, including the development of neuroinflammation assays and the optimisation of our compounds' target engagement in the brain."

Drug Discovery Manager at Parkinson's UK



In 2022, **NRG Therapeutics**, an innovative neuroscience company targeting mitochondrial dysfunction, and **Domainex**, announced a collaboration focused on developing novel small molecule disease-modifying medicines for the treatment of Parkinson's disease, motor neuron disease (MND) and other debilitating chronic neurodegenerative disorders. Domainex, is providing fully integrated lead optimization services including assay biology and medicinal and computational chemistry.

www.nrgtherapeutics.com

"We chose Domainex as our lead CRO partner to support the lead optimisation phase of a neuroscience project funded by a Biomedical Catalyst Award from Innovate UK. Excellent progress has been made by the medicinal chemistry and biology teams at Domainex, and the project is on track to deliver its next milestone."

Dr Neil Miller - CEO, NRG Therapeutics

Partners



Domainex is an award winning, fully integrated drug discovery CRO, serving biotechnology and pharmaceutical companies, and patient foundations globally. Our scientists have worked on numerous CNS programmes at all stages of preclinical research from hit identification through to candidate nomination.

By focussing on key physicochemical properties of molecules such as size, polar surface area, lipophilicity, pKa and the number of hydrogen bond donors, compounds can be designed which have a greater likelihood of reaching the brain. The integration of *in silico*, *in vitro* and *in vivo* data leads to improved understanding in order to better predict and optimise the brain exposure for neurological targets.

www.domainex.co.uk



Cresset Discovery is a premier computational chemistry CRO with a proven track record delivering high impact drug discovery projects. From ideation to synthesis and biological results, their expert CADD scientists are the best at what they do. Working alongside you from the ground up, they apply the best *in silico* techniques, and give expert advice and guidance, to accelerate your assets through the pipeline.

www.cresset-group.com/discovery



Metrion Biosciences is a sector-leading contract research organisation specialising in preclinical ion channel drug discovery research services.

Metrion delivers comprehensive drug discovery outsourcing solutions to pharmaceutical and bioscience customers worldwide; all from a single, state-of-the-art UK-based research hub.

www.metrionbiosciences.com



Pharmidex is a UK-based CRO founded in 2002 providing high quality, cost-effective and rapid solutions to clients in *in vitro* ADME, Pharmacokinetics (DMPK), bioanalysis (non-GLP, GLP/GCP) and toxicology (non-GLP, GLP). Pharmidex also offer efficacy models supporting oncology, CNS, respiratory, stroke and auto-immune disease programmes.

www.pharmidex.com



Location of partner companies

All our partners are located in the Cambridge area and within 40 miles of each other. The benefits of being closely located include:

- **Rapid Design-Make-Test cycle times**
- **Teamwork & Communication**
 - The ability to regularly meet face-to-face for project meetings and partner steering groups
- **Reduced shipping times** and **environmental impact** compared to overseas shipments.



About Domainex

Domainex is a fully integrated drug discovery service company based at Cambridge, UK. We serve pharmaceutical, biotechnology, academic organisations and patient foundations globally. We have ambitious growth plans and are expecting to reach 110 biologists and chemists in the near future. We provide integrated services, from disease target selection to candidate drug nomination. We have a very strong reputation for contributing innovative ideas, undertaking high-quality experiments and for generating intellectual property on behalf of our clients. We strive to build strong, dynamic relationships. In 2022, we served over 90 clients from the UK, Europe, the United States, Japan and Australia and had a project renewal rate of over 80%.

How Can Domainex Help Your Drug Discovery Project?

Our highly experienced, multi-disciplined scientists – molecular biologists, protein biochemists, assay biologists, structural biologists, medicinal, computational and bio/analytical chemists, *in vitro* pharmacologists and ADME scientists – will support you to advance your drug discovery projects towards drug development effectively and efficiently. We provide customised programmes to address your specific needs at each stage of drug discovery. We draw from a wealth of expertise built up over the last 20 years across a wide range of drug targets and therapeutic areas. From our sites within Europe's leading bioscience hub at Cambridge, UK and with access to the very latest cutting-edge technologies, we are able to help you realise your goals and enrich your discovery pipeline.

Contacts

If you would like to know more about Domainex's discovery services, or speak to us regarding your own drug discovery needs, please contact us at: enquiries@domainex.co.uk

Alternatively we can be contacted directly as follows:

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