**AstraZeneca-Funded Non-Clinical PhD Studentships**

**Expression of Interest**

**Remit**

The aim of this programme is to fund 3.5 year Non-Clinical PhD studentships at the University for talented graduates in research areas which align with the strategic interests of AstraZeneca. These areas of interest are included at the end of this document (appendix 1) and align with the research priorities of the Biologics Engineering, Discovery Sciences, Oncology Machine Learning & AI, Data Sciences & AI, Global Chemistry Network, Biopharmaceutical development, Early cardiovascular, renal and metabolic therapy areas, Clinical Pharmacology and Safety Sciences, Respiratory and Immunology research areas of AstraZeneca

**Eligibility**

All applications should be submitted as a partnership between identified Principle investigators employed by the UoC and AZ.

Individual investigators should identify an AZ/Cambridge partner before submitting their project. The programme management team can assist with the identification of a suitable partner, please see below for programme management contact details. The University of Cambridge Principal Investigator will be the lead investigator for this studentship should it be awarded. Support for the proposal will be required from the relevant University of Cambridge Head of Department prior to submission

**Reporting**

A non-confidential annual progress report will be requested for submission to the Steering Committee. The main point of contact will be the University of Cambridge Program Manager. It is expected that the program manager will be kept updated on the progress and any changes in circumstances regarding the AZ-funded non clinical studentships.

**Review**

Proposals will be reviewed by the Steering Committee which includes representation from AstraZeneca and the University of Cambridge. The Committee will be responsible annual allocation of studentships based on proposal fit to strategic remit, the enhanced collaborative potential of the proposal, and available budgets.

**Funding**

Programme funding for non-clinical PhD studentships covers student stipend, tuition fees (at Home fee level only) and an allocation towards project consumables and training (See appendix 2). Once studentships have been awarded, each department will be responsible for the recruitment and integration of the student with the support of the Cambridge Programme Manager.

**Contact details**

All proposals should be submitted by email to the programme managers:

University of Cambridge: Meghana Patel (meghana.patel@admin.cam.ac.uk)

AstraZeneca: Michael Tonge (Michael.tonge@astrazeneca.com)

**Deadline**

The deadline for receipt of full proposals is **Monday 22nd August 2022.** As timelines are quite tight, PIs are strongly encouraged to seek a collaborative partner as soon as possible (and prior to 01st Aug 2022) so that full submissions can be made to the selection committee by the specified deadline.

**Expression of Interest for AZ-Funded Non-Clinical PhD Studentships**

|  |  |
| --- | --- |
| **Title of project** |  |

**UNIVERSITY OF CAMBRIDGE PARTNER DETAILS -**

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| **University lead investigator(s)** |  |
| **E-mail address** |  |
| **Department/School** |  |
| **Link to webpage** |  |

**ASTRAZENECA PARTNER DETAILS – \***If none, please contact the Cambridge Programme Manager as soon as possible and before 01st August 2022.

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| **Industry lead investigator(s)\*** |  |
| **E-mail address\*** |  |
| **AZ Department(s) which align with proposal (delete as required)**  | Biologics Engineering / Discovery Sciences / Oncology Machine Learning & AI / Data Sciences & AI / Global Chemistry Network Biopharmaceutical development, Early CVRM, Clinical Pharmacology and Safety Sciences, Respiratory and Immunology research areas |
| **AZ broad area of research alignment - Please indicate, from list at the end of this document, which areas you have most interest in working with or where strongest alignment exists with your research/proposal** |  |

**PROJECT DETAILS**

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| **Background and hypothesis** *200 words, non-confidential detail ONLY:* |
| Click or tap here to enter text. |

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| **Proposed experimental approach***500 words, non-confidential detail ONLY; Please include envisioned timeline for studies in years 1-3:* |
| Click or tap here to enter text. |

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| **Expected key outcomes** *Up to three bulleted outcomes* |
| Click or tap here to enter text. |

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| **Key publication(s) linked to research proposal***List up to 5 publications which relate directly to the proposed project. This information may be used to align AstraZeneca/Cambridge collaborators.* |
| Click or tap here to enter text. |

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| **Enhanced potential through collaboration***Please outline the advantages to this project proposal and the student of working in collaboration with an AstraZeneca/Cambridge partner. Please include details such as individual expertise / facilities / etc. 300 words max.* |
| Click or tap here to enter text. |

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| **What proportion of the studentship would you envision the student spending at the partner institution?** | University of Cambridge: |
| AstraZeneca:  |

**Please note:** Full proposal submissions will require input and agreement from both AstraZeneca and Cambridge project supervisors

**University of Cambridge partner**

PI (Name) PI (Signature) Date

Head of Department\* (Name) Head of Department\* (Signature) Date

\**or delegate in charge of Graduate Studies*

**Astra Zeneca partner**

PI (Name) PI (Signature) Date

**Timeline of events for project and candidate selection – non-clinical**

1.            **8th July 2022: Call for expressions of interest open**. EoI documents circulated at both Cambridge and AstraZeneca based on broad areas of need defined by AstraZeneca. For Cambridge or AstraZeneca researchers requiring a collaborative partner, the AstraZeneca Programme Manager and the Cambridge Programme Manager will coordinate to seek out potential partners and make connections. As timelines are quite tight, PIs are strongly encouraged to seek a collaborative partner as soon as possible (and prior to 01st Aug 2022) so that full submissions can be made to the selection committee by the deadline.

2.            **22nd August 2022: Closing date for receipt of full proposals**. Research proposals are submitted to the non-clinical committee for approval based on available budget for the coming cohort. Research project proposals to be submitted to the committee following approval from respective Cambridge departments. University of Principal Investigators will be responsible for departmental approval.

3.            **3rd September 2022: Committee project selection**. Non-clinical committee to review and approve all proposals and determine the final studentships to be advertised and recruited for.

4.            **13th** **September 2022: Project advertisement.** Studentships to be advertised as soon as possible following selection by the non-clinical committee and the lead taken by individual departments with support from the Cambridge Programme Manager.

5.            **31st October 2022: Deadline for applications**

6.            **11th November 2022: Application shortlisting.** The shortlisting will be carried out by the academic and industrial project supervisors. Members of the non-clinical committee reserves the right to participate in candidate shortlisting and selection process. Candidates will be shortlisted based on merit and then required to submit application on CamSIS.The Cambridge Programme Manager will be informed of the outcome asap.

7.            **1st December 2022: Applicant interviews**. The interviews will be carried out by the academic and industrial project supervisors. Members of the non-clinical committee reserves the right to participate in candidate shortlisting and selection process. The Cambridge Programme Manager will be informed of outcome asap.

8.            **Dec 2022 – Feb 2023: University applications completed**. The Cambridge Programme Manager will liaise with individual departments to ensure successful applicants are guided through the registration process and set up of budget allocations.

9.            **Dec 2022 - September 2023: Studentship agreements**. The Cambridge Programme Manager will work closely with AstraZeneca and Cambridge PIs, as well as associated contracts teams to ensure that studentship agreements are drafted and finalised in a timely manner.

10.         **October 2023: Project commencement**. Students begin Term 1 of their studentship.

**Appendix 1: AstraZeneca Strategic Areas of Interest**

When submitting your expression of interest, please indicate in the relevant section above both the AstraZeneca Department(s) and specific AstraZeneca Area(s) of Interest which most closely align with your research.

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| **AstraZeneca Department** |  **AstraZeneca Area of Interest** |
| **Biologics Engineering (BE)** | Biologics engineering (BE) is a department within the Oncology business unit of AstraZeneca. BE is responsible for the isolation, optimisation and characterisation of the majority of biologic drugs within the AstraZeneca organization. The department focuses on antibody discovery using various platforms including phage/ribosome display and immunization, optimization of Abs and protein engineering, peptide discovery, multi-specific abs, assays and screens. Areas of primary interest* + in silico design using artificial intelligence algorithms to predict changes to improve Antibody properties
	+ de novo protein scaffold design
	+ Predictive tools for surface properties and biophysical properties of proteins
	+ Mechanisms for exploring structure-function relationships
	+ Technologies supporting antibody-drug conjugates
	+ Cell/organ targeting agents for payloads, oligos and other Abs (especially , heart, lung, kidney)
	+ B cell isolation technologies
	+ High throughput assays and/or multiplex systems especially anything microfluidics related
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| **Discovery Sciences (DS)** | Discovery Science – areas of primary interest:1. Machine Learning (ML) /Artificial Intelligence (AI)* Applied to cellular imaging for e.g. identification, secondary pharmacology and mechanistic understanding
* Applied to Nucleic or amino acid data for e.g. structural prediction
* For diverse information sources on e.g. graphs

2. Mechanistic understanding of target-ligand interactions from molecular to cellular level:* Understanding cellular and molecular mechanisms, including cellular trafficking of Oligonucleotides, by exploiting synergies between structure, biophysics, biochemistry and molecular and cellular biology
* Particular interest in the study of multi-protein and ternary mediated complexes in physiological target contexts. (for example, PROTAC, epigenetics, etc.)
* Affinity screening at scale in cells, including using label free technologies

3. Gene Editing* How do we improve in vitro and in vivo editing of genomes?
* From understanding of modulation and characterization of DNA repair/recombination pathways for optimal gene editing to development of greater scale and/or efficient systems. Including predicting and analysing on-target editing outcomes.
* How do we improve the tissue specific in vivo/therapeutic delivery (efficacy) of editing enzymes?

4. In vivo expression of biologics* How can we improve the use of DNA, RNA and AAV to deliver therapeutics and vaccines to the patient, through sequence or capsid engineering?
* Understanding how DNA, RNA and AAV interact with the innate immune system and how we can reduce the impact in patients
* Understanding how DNA, RNA and AAV are transported within the cell to enable expression
* Developing molecular switches to control the expression of therapeutic DNA and AAV

5. Multi-omics and genomics based research* Investigating links between phenotypic traits and variation in biological systems and processes to improve disease relevance in preclinical and animal models.
* Integration, interrogation, and analysis across -omics datasets such as those generated by multiple omics technologies
* Develop and apply innovative analytical approaches to integrate human genomics data with detailed clinical, biomarker and -omics data to advance understanding of disease biology and identify novel therapeutic strategies for diseases with unmet medical needs

6. In vitro and in vivo models that recapitulate disease aetiology* Including 3D systems and stem-cell derived organoid models and analysis thereof
* Miniaturised cell model systems
* Automation processes for assay generation and screening
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| **Oncology Machine learning and AI****(Onc. ML/AI)** | High-level areas of interest from across Oncology R&D1. Data aggregation from various sources (clinical, multiple different imaging, etc.) to produce patient risk scores. (Paul Metcalfe & Gunter Schmidt)
* How should we best integrate multiple different data sources to derive understanding of potential patient outcomes?
* What is the value of information in each of the different data sources?
* What tests should be done in a patient in what order to maximize useful information gain?
* Causality: how can we put a plethora of data modalities together to make robust causal inferences.
1. Machine learning in high noise environments (Paul Metcalfe)
* The typical ML application has a high signal-to-noise ratio; in the clinical world life is much more stochastic.
* How do we maximise the utility of ML tools, and understand the distributional uncertainty around any prediction (i.e. distributional learning)?
1. Methodologies for natural language learning, de novo creation of ontologies, information extraction from text (Subha Mahdevan)
2. Human factors: storytelling, visualization, best practices and effective communication of data (Subha Mahdevan)
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| **Data Science and AI (DSAI)** | The following are the core areas of interest for DSAI1. Machine learning research (Shameer Khader)

• Computational phenomics • Digital Drug (Re)positioning• Application of AI in Translational Bioinformatics• AI-guided Precision Medicine• Disease stratification and sub-typing (accelerated phenotypes) • Computational systems biology using biological networks and graph-based analytics for target/therapeutic discovery and repositioning • Tool/methodology development using biomedical and clinical trial data repositories (SAEgnal, Omicsfold, OSPred, StarGazer, ClinicalTrials2Vec, TrialGraph etc.) 1. Sensors and Wearables (Glynn Dennis)

• Novel phenotypes using deep learning 1. Clinical Trial Analytics (Hrishikesh Karvir)

• Predictive modeling to improve clinical trial operations(site selection, clinical trial enrolment etc.) 1. Biological Knowledge Analytics (Jonathan Mangion)

• Bioinformatics analytics • Multi-omics analytics for target, pathway and drug discovery 1. Healthcare informatics and Visual Analytics (Shameer Khader – interim lead)

• Real-world data-driven analytics • Integrating of RWD/RWE with AI approaches 1. Machine learning and Image Analytics (Claire Donoghue)

• Computer vision approaches to improve disease diagnoses • Deep learning for pathology • Radiomics |
| **Global Chemistry Network (GCN)** | The following are areas of research interest for the global chemistry network at AstraZeneca 1. Innovative Synthetic chemistry with applications to drug discovery and process development
* Development of novel synthetic methodologies with medicinal and process chemistry relevance (e.g. Photoredox, C-H activation, Late stage C-H (sp3) functionalization, heterocyclic chemistry, atropoisomer chemistry, catalysis, biocatalysis, non-natural amino acid synthesis).
* Synthetic methods to enable environmentally friendly manufacture (e.g. Reactions in water, novel green solvents, sustainable catalysis).

 1. High throughput experimentation and reaction optimisation with application to drug discovery and process development
* Reaction optimisation and discovery using high throughput experimentation
* Efficient HT analytical characterization of HTE experiments and automated data analysis including automated quantification techniques and nanoscale analysis.
* Data capture and processing methods of HTE/reaction data for AI/ML predictions
* Automated chemistry (including in air chemistry)
* Computational methods,  machine learning mechanistic modelling, process analysis and kinetics.
* Approaches for the optimization of reactions, including mechanistic modelling, process analysis and kinetic studies.

 1. Innovative Chemical Biology
* Proposals bringing additional understanding, improved processing or alternative approaches to species such as peptides, oligonucleotides, antibodies, ADCs, dendrimers and polymer conjugates.
* PROTACS and protein degradation, cellular uptake through active transport.
* Bioconjugation and modification chemistry for oligonucleotides and proteins. Covalent targeting of proteins.
* Understanding Oligonucleotide physical properties.
* On DNA compatible chemistry
* New methods to predict protein and RNA 3D structure and functional binding sites
* Stapling chemistry on peptides
* Ways to find functional small molecule binders to lncRNA

 1. Novel analytical and computational methods
* Predictions of crystalline solubility from 2D structure
* Innovative and improved computational methods such as affinity and free-energy of binding predictions, conformational sampling, and identification of cryptic / allosteric pockets in proteins
* Innovative analytical methods with medicinal chemistry relevance. For example, novel biomimetic chromatography; label-free technologies, quantification of in-cell drug concentrations
* Development of the underlying analytical methodologies required to characterise and understand the properties of an increasingly diverse range of compounds, including all those outlined above, in addition to improved analysis for small molecules.

 1. Novel Process Chemistry
* Improvements to isolations and drying of drug substances and intermediates
* Physical aspects of processing, including work-ups and fundamental understanding of physical properties of drug substances and intermediates
* Understanding and modelling of crystallisation
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| **BioPharmaceutical Development (BPD)** | BioPharmaceutical Development (BPD) provides end-to-end biologics development capabilities to produce stable and effective therapies that enable clinical studies and commercial supply – delivering value to patients & strategic advantage to our diverse portfolio. The following are examples of areas of research interest for BPD:1. Understanding the protein products of RNA based therapeutics, e.g. What differences arise in protein yield and post-translational modifications given different cellular expression systems and how does this differ across time-points after treatment?
2. How to deliver high subcutaneous doses of biopharmaceutical drugs through for example stabilising high concentration protein formulations, and prediction/modelling of their bioavailability post administration.
3. Improving development of mab-based therapeutics e.g. Mechanistic understanding of and improving expression and product quality (e.g. aggregation) of mab-based therapeutics such as bi- and multi-specifics through molecules and cell engineering
4. AAV research
5. Gene therapy research
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| **Early Cardio Vascular, Renal and Metabolism Therapy area (CVRM)**  | The early CVRM therapy area group have primary research interests in the areas of:1. NASH and non-NASH liver disease
2. Diabetes
3. Obesity and novel mechanisms of weight loss
4. Lipodystrophy and “Fat Failure syndrome”
5. In vitro/in vivo modelling of human metabolic disease
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| **Clinical Pharmacology and Safety Science (CPSS)**  | The toxicities in key organs demand deep understanding of the biology of those organs to define potential adverse events. Research that delivers on the cellular and genetic mechanisms of the heart, liver, lung, kidney, skin and gut alongside broader diffuse tissues such as the blood and wider immune system is of interest. In particular: * Mechanistic understanding of perturbation of human physiology and cell biology (particularly with the heart)
* Understanding how genetics influences human physiology (particularly heart, liver, lung)
* Understanding of the immune system and immune cell-cell interactions within key areas of interest (lung, gut, skin – the interface with the outside world)
* Deep understanding of immune signalling and cell stress responses (unfolded protein response, pathogen detection etc) – deployment of omics and imaging methodologies to understand cell behaviours, activation etc
* Influence of drug toxicities on the bone marrow
* Immunogenicity and drug hypersensitivity
* The utility of complex, multicellular in vitro models to address adverse drug reactions and toxicities
* Context of disease with drug toxicities

From an imaging and mass spec approach there is interest in projects across a broader area of focus, studying the complexity of events occurring in all biology but applying the approaches below: * Exploring research themes that bridge ‘omics endpoints.
* Maximize data that can be generated from every sample.
* Deployment of novel or emerging technology and related data integration and mining
* Interactions in tissue microenvironment

A key focus here is on data generation and handling, deep dives into specific questions and deep profiling of adverse toxicity findings. |
| **Respiratory and Immunology (R&I)**  |

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| Topic area of Interest: * Airway biology and immunology
* Regenerative biology and aging and models thereof.
* Understanding of Key Mechanisms in COPD
* In vivo imaging of COPD
* Molecular factors in lung epithelial cell function
* Macrophage biology and TLR, T cell biology  epigenetics,
* Identification and characterization of mechanisms to maintain and restore epithelial barrier integrity
* epithelial innate immunity
* cellular senescence
* Immune-mediated control of epithelial integrity
* upper respiratory tract sampling methods for IL-33/ST2 pathway activity
* Role of IL-33
* Aging
* Immunology
* Microbiology
* Pharmaceuticals
* Regenerative Biology
* RRR
* Systems Biology
* Stem Cells
* Structural Biology
* Technology Development

More specific * mathematical modelling of single cell omics and the biological network analysis.
* understanding cell trajectories, statistical modelling of cell heterogeneity and its implication on required sample sizes and stability of cell clusters,
* multi-omics integration building e.g. regulatory gene networks based on miRNA, RNAseq and protein data.
* Prediction of protein structures, functions and interactions (from amino acid sequences)
* Prediction and experimental verification of the effects of mutations on protein folding and function
* Development of algorithms for the evaluation of the quality of 3D models of proteins and setting data standards for theoretical model validation
* PPI databases, exploitation & visualization
* Unravelling structure-function relationships of proteins and protein-ligand complexes, investigating molecular mechanisms, drug and vaccine development
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Appendix 2: Studentship funding breakdown

Please note, the AstraZeneca funded non clinical studentship program covers academic fees for **UK/home students only**. Any additional funding required for the recruitment of overseas students will not be covered and will have to be met by the University department or other sources.

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| --- | --- | --- | --- | --- |
|  | **Year 1** | **Year 2** | **Year 3** | **Year 4** |
| Student stipend | (£)19500 | (£)20100 | (£)20700 | (£)21350 |
| Combined fees (Home students only) | (£)9111 | (£)9111 | (£)9111 |   |
| Consumables | (£)11000 | (£)11000 | (£)11000 |   |
| T&S | (£)1500 | (£)1500 | (£)2000 |   |