1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

**Name of the English NHS Provider/University Partnership:**
UCLPartners Academic Health Science Centre

**Name, email and telephone number of the Lead Contact for the proposed AHSC:**
*Note: This will be the contact for all correspondence relating to this application.*

**Name:** Professor Sir John Tooke, Academic Director, UCLPartners  
**Email:** j.tooke@ucl.ac.uk  
**Telephone Number:** +44 (0)20 7679 0878

Please list the members of the partnership involved in the proposed AHSC, including names of NHS Provider(s) and university(ies) involved:

At the core of UCL Partners (UCLP) AHSC are our Biomedical Research Centre (BRC)/Biomedical Research Unit (BRU) strengths and associated specialist service provision. To strengthen our contribution further, we propose to embrace programmatic links with neighbouring institutions with specific expertise that build on this model.

**Accordingly, the proposed members of the AHSC are:**

**Universities:**
- University College London (UCL)  
- Queen Mary University of London (QMUL)  
- The London School of Hygiene and Tropical Medicine (LSHTM) (Infection, Immunity and Inflammation Programme and global links)

**NHS Trusts:**
- University College London Hospitals NHS Foundation Trust (UCLH)  
- Great Ormond Street Hospital for Children NHS Foundation Trust (GOSH)  
- Moorfields Eye Hospital NHS Foundation Trust (Moorfields)  
- Royal Free London NHS Foundation Trust (RFH) (Infection, Immunity and Inflammation Programme)  
- Barts Health NHS Trust (Barts) (Cardiovascular Programme)
Governance

UCL Partners (UCLP) is a single registered company, coordinating the activities of our Academic Health Science Centre (AHSC), Academic Health Science Network (AHSN), and associated Collaboration for Leadership in Applied Health Research and Care (CLAHRC), Comprehensive Local Research Network (CLRN) and Local Education and Training Boards (LETB). The AHSC is accountable through the Academic Director to the AHSC Board involving the CEOs of the partner institutions and chaired by the UCLP MD.

Geography

AHSC partners are co-located in London within a radius of 3 kilometres.

Education

Lead provider for all doctors in training in North Central and North East London (over 4,000 posts) delivering education programmes aligned with the AHSC, AHSN and CLAHRC strategic objectives.

Research

AHSC draws together research excellence across three world-class universities. Three BRCs and two BRUs increasingly operate as an integrated ‘portfolio’. In 2014 a single Clinical Research Network will be created connecting the AHSC to 6 million patients.

Patient Care

Single sites for specialist cancer*, cardiac*, ophthalmic, paediatrics & adolescents, and major trauma, within integrated systems (*subject to public consultation).

Informatics

Single Informatics Board, Independent Chair and Chief Clinical Information Officer (CCIO) Single e-Health strategy for clinical data sharing and a single academic platform, Farr Institute @ UCL, across all partners.

2. ABSTRACT (250 words)

In plain English, present the specific aims, goals and objectives of the proposed AHSC.

Our Goal is to create an unparalleled AHSC that harnesses our academic strengths, partnerships and industrial links to the fullest extent to improve the health and wealth of society.

To achieve that goal we aim to pursue six Programmes that map onto our Biomedical Research Centre and Unit strengths and related specialist services, underpinned by world class informatics capability and economic growth platforms.

All programmes will develop world class educational provision to address both current and future health and scientific need as well as streamlined translational pathways from discovery through to the development of novel diagnostics, therapeutics and prevention strategies.
Specific Programme objectives include:

- Neuroscience: advancing treatments for neurological disease, sensory loss and mental illness
- Child Health: advancing therapeutic innovation for rare, congenital and developmental diseases
- Infection, Immunity and Inflammation (III): tackling the continuing global threat of infection and antimicrobial resistance and the dual challenge of deficient and inappropriate immunological response
- Cancer: advancing precision medicines for cancer and preventative strategies based on a deeper understanding of DNA mutations, tumour evolution and the immune system
- Cardiovascular: developing preventative strategies, therapeutic target validation and advanced/bespoke device development
- Eyes and Vision: leading therapy advances for the most common blinding conditions

To ensure our research outputs, educational advances and service innovations have maximum impact we aim to fully utilise the seamless integration with our Academic Health Science Network, subserving a population of 6m, and our extensive global networks.

3. STRATEGY (4 pages)

Please provide the strategy for how the alignment of strategic objectives will continue to improve health and healthcare delivery including:

- A restatement of the partnership’s goals, vision and purpose;
- Specific overall short (1-2 years), medium (2-3 years) and long term (4-5 years) objectives for the AHSC;
- A summary of the partnership’s top six specific themes or work Programmes of focus and how they fit into the overall strategy and goals of the proposed AHSC;
- An outline of the expected specific deliverables of the AHSC over the 5 years of designation that could not be achieved through another type of partnership;
- How success of the proposed AHSC will be evaluated, including success against specified objectives and deliverables;
- Evidence that the partnership has a strong clinical informatics platform to underpin the delivery of the proposed AHSC objectives;
- How the partnership will further align NHS provider and university strategic objectives in order to harness and integrate world-class research, excellence in health education, and excellence in patient care over the 5 years of designation. How this will lead to improved health and healthcare delivery, including through increased translation of discoveries from basic science into benefits for patients.

Since designation, our AHSC has achieved: an average 8% per annum increase in research grant income; 21% increase in highly-cited publications; been re-awarded 3 BRCs and a BRU, and awarded a further BRU in dementia; the status of hosting the university with the greatest number of industry partnerships in the UK.

Our Purpose is to harness discovery science and use the focused strengths of our BRCs and BRUs and our clinical trial and informatics capabilities together with educational expertise to translate research into world-class clinical outcomes and population health and wealth gain.

Our Goal is to create an unparalleled AHSC that is the engine of a streamlined translational pathway. We will engage an interdisciplinary mix of academics, clinicians and industry leading to improvement in health locally, nationally and globally through advances in prevention, diagnostics and therapy.

Our Vision is to achieve a step function in performance and set a new benchmark for what can be achieved by an academic health alliance, configured to exploit synergistic strengths in six programmatic areas where we have specialist and academic expertise, and an established culture of collaboration.

Our Approach to achieving our Vision will be: i) a relentless focus on excellence, exploiting the constituent strengths and commitment to partnership working across our AHSC, fostering multidisciplinary working and industrial engagement; ii) a focus on innovation, bringing interdisciplinary academic excellence to bear on the most pressing health problems of our day, and developing our strategy and workforce capability to address these; iii) realising our full potential in the burgeoning fields of personalised medicine, lifelong health and informatics; iv) providing the outputs to fuel innovation, wealth generation, and healthcare quality
improvement locally, nationally and internationally; iv) integrating our AHSC activities with those of our AHSN to ensure diffusion of our outputs whilst ensuring clear, robust governance of our AHSC functions. The AHSC governance arrangements include the creation of Research, Education, Care Quality and Wealth Generation Sub Boards to drive the delivery of the specific overall short, medium and long term objectives for the AHSC:

**Research:**
*Short term:* (i) Metrics to drive performance/interdisciplinarity; (ii) create cross-cutting initiatives to support all Programmes that align with UCL’s multidisciplinary pan-faculty, pan-Partnership research networks (Personalised Medicine, Life Long Health and Informatics research ‘Domains’); (iii) enhance Programme coordination support; (iv) exploit UCL’s ‘Frontiers Domain’ to anticipate the advance of cutting-edge science.

*Medium term:* Secondment of AHSC clinician scientists to the Francis Crick Institute and creation of ‘satellite’ Francis Crick Institute groups within UCL discovery teams/BRC/U and physical sciences, maths and engineering.

*Longer term:* (i) Forge stronger interdisciplinary links with Oxford and Cambridge Universities in addition to the London AHSCs, including promotion of the ‘M11 corridor’ as an axis for biomedical science excellence; ii) establish at least one further national and one further international partnership per Programme with other world-class centres of excellence with complementary strengths; iii) achieve world-class outputs (top 10 or better) in all Programmatic areas.

**Education:**
*Short term:* (i) Commence recently awarded Wellcome Trust Clinician Scientist PhD programme, BRC/U PhD Crick programme, Bioinformatics PhD and new undergraduate degrees in Population Health Sciences and clinical science; (ii) establish UCLP Quality Improvement Fellows joint with LETBs.

*Medium term:* (i) Undergraduate medical programmes adapted to accommodate ‘precision medicine’; (ii) introduce multi-professional modular Masters Programmes in genomics, molecular pathology, bioinformatics and improvement science; (iii) roll out Academic Careers Office provision across Partnership.

*Long term:* Research awareness raising and critical appraisal skills permeate all Programmes.

**Wealth Generation:**
*Short term:* (i) Monitor relevant metrics; (ii) transplant three ‘industry ready’ projects for the Stevenage Bioscience Catalyst; (iii) collaborate with London AHSCs to develop and project London Life Sciences networked capability; (iv) diffuse UCL’s successful Translational Research Office and intellectual property (IP) exploitation processes across the AHSC; (v) create a Wealth Generation Sub-Board with industrial and investment input; (vi) use our Centre for the Advancement of Sustainable Medical Innovation (CASMI) to enhance the innovation pipeline.

*Medium term:* (i) Select three further ‘industry ready’ projects for the Stevenage Bioscience Catalyst; (ii) establish bi-directional secondment partnerships with at least one major pharma company per Programme; (iii) generate research publications and policy reports from CASMI.

*Longer term:* Establish major discovery partnerships for each Programme, mirroring current arrangements, with e.g. Eisai (Neuroscience), GlaxoSmithKline (GSK) (III, Eyes and Vision) and Pfizer (Eyes and Vision).

**Care Quality:**
*Short term:* (i) Adoption and promulgation of the pan-Partnership quality scorecard; (ii) systematic application of best practice public and patient involvement (PPI) across Programmes to ensure patient perspective informs all initiatives; (iii) outcome monitoring (National Institute for Cardiovascular Outcomes Research (NICOR), Public Health registries); (iii) forge close links with newly-established Collaboration for Leadership in Applied Health Research and Care (CLAHRC) to inform research agenda; (iv) establish national networks in areas of specialist expertise (e.g. rare diseases); (v) become anchor partner in the Commonwealth’s ‘Common Health’ initiative, sharing quality improvement strategies and evidence based practice across the Commonwealth.

*Medium term:* Introduce health informatics to subserve major integrated pathways aligned with Programmes.

*Longer term:* Achieve demonstrable improvement in at least one key outcome measure per Programme, attributable to therapeutic advance/service innovation led by the AHSC.

**Summary of the partnership’s top six Programmes and how they fit into the overall strategy and goals of the proposed AHSC:**
Our BRCs/BRUs play a critical role in the translational pathway. Their award evidences our strength in six major areas with related specialist clinical expertise. Our AHSC will focus its Programmes on these six areas, linking discovery science and clinical trials activity with these engines for experimental medicine with growing industrial links, whilst drawing on our exceptional population health science capabilities to effect ‘reverse translation’. The goal of all Programmes is to achieve major health improvement through advances in prevention, diagnostics and treatment. To achieve the transformative change in AHSC performance to which we aspire, effort in these six Programmes will be supported by three cross-cutting initiatives: Informatics, Personalised Medicine, and Lifelong Health and close attention to the overall objectives of the AHSC.

**Neuroscience**
The Neuroscience Programme draws on world class capabilities to address some of the most challenging
health problems of our time: mental health exploiting a multidisciplinary approach combining insights from basic neuroscience, clinical and epidemiological psychiatry and clinical psychology to devise new treatment and resilience enhancing paradigms; understanding and influencing human behaviour, drawing on expertise in behavioural and cognitive sciences and neuroscience to improve understanding of the basic neural and cognitive processes underpinning human well-being across the life course; neurodegeneration and neuroprotection, applying integrative molecular, cellular, neuroimaging, epidemiological and cognitive approaches to neurodegenerative disorders to define disease, illuminate pathogenesis, and particularly guide design and evaluation of therapeutic interventions in the new Leonard Wolfson Experimental Neurology Centre; and sensory systems and therapies, combining expertise in audition and cognition to transform understanding of the mechanisms underlying sensory systems, dysfunction and developing and validating new therapeutic approaches, from stem cells to neuroprosthetics.

Child Health
The Institute of Child Health, with its clinical partner GOSH, is one of the world’s leading children’s academic medical centres focused on improving the health of children and the adults they will become, building on excellence in rare diseases research and clinical care. Using unique patient cohorts, deep phenotyping, next generation sequencing, multi-omics data cell and gene therapies, we will pursue six themes: Genetics & Genomic Medicine; Developmental Biology & Cancer; Developmental Neurosciences; Infection, Inflammation & Immunity; Cardiovascular; Population, Policy and Practice, all integrating as appropriate with other AHSC programmes. By drawing together biomedical science and population research expertise, we will increase translational potential and deepen understanding of the formative influence of childhood on lifelong health.

Infection, Immunity and Inflammation (III)
This Programme, drawing on the Institute of Immunity and Transplantation (Royal Free Hospital London) and the Bloomsbury Research Institute (UCL/LSHTM pathogen research), underpinned by next generation molecular and functional diagnostics and our informatics expertise, will address: Immune intervention to treat disease and/or establish tolerance, including infection, cancer; auto immune diseases including inflammatory bowel disease and type I diabetes; and tolerance to artificial organs. Infection prevention and control will embrace early warning indicators, genomic science to track and control outbreaks, host/pathogen interactions as therapeutic targets and antibiotic resistance. Inflammatory conditions will target the development of novel therapies such as amyloidosis, scleroderma and rheumatoid arthritis.

Cancer
By exploiting UCLP’s Integrated Cancer Service, London Cancer, the Cancer Programme will improve early diagnosis and treatment of at-risk patients through application of behavioural science and bio-behavioural interventions; advance prediction and stratification, developing genomic and epigenetic approaches to track tumour heterogeneity; develop novel treatments, targeting cell death-receptor systems and immune regulation; develop technology to understand (e.g. new imaging modalities in conjunction with KCL and Imanova) and treat (e.g. Proton beam) all phases of cancer; play a leadership role in advancing cancer clinical trials.

Cardiovascular
The Cardiovascular Programme will exploit UCLP’s integrated care pathway and the new specialist hub to drive advances in: diagnostics, utilising genomics in rare inherited disease (e.g. cardiomyopathy) and commoner conditions (e.g. dysrhythmia, hypertension); target validation and therapeutic innovation drawing on Mendelian Randomisation, deep phenotyping, molecular physiology, pharmacology and advanced imaging; novel device based diagnostics and therapies (in partnership with Yale) e.g. renal denervation, imaging atlas of CV disease for prototype optimisation; prevention evaluation and ‘real world’ trials using the Farr Institute @ UCLP and outcome registries (NICOR); and research capability through developing a UCLP Translational Cardiovascular Academy, engaging the Francis Crick Institute.

Eyes and Vision
Moorfields and the Institute of Ophthalmology are at the heart of an international collaborative venture to address major causes of blindness including retinal disease, glaucoma and corneal and eyelid disease using the following technologies and expertise: regenerative therapies and novel drugs; gene therapy; diagnostic and surgical novel devices; imaging and functional assessment of the eye; ocular inflammation and infection. These sub-themes will be underpinned by genotyping/phenotyping and informatics, including Open Eyes, an open-source electronic patient record system with global reach.

Expected AHSC deliverables that could not be achieved through another type of partnership:
A particular feature of our partnership is our close integration with our AHSN, whilst recognising the distinctive role that the AHSC plays. Such integration has enabled us to achieve the following advances for our AHSC mission that will be fully exploited over the next five years, progress that we believe would be difficult to replicate with a less seamless structure:

- The adoption of a pan-partnership, informatics platform covering a population of six million, to drive both service improvement/attention to individual care needs as well as research and its translation. Our establishment as one of the four hubs of the National Farr Institute for Health Informatics Research (the Farr Institute @ UCLP) draws on the strengths of all three academic partners (UCL, LSHTM and QMUL).
We will harness that capacity and the support of constituent institutions across our AHSN to develop replicable informatics solutions, commencing with our six Programmes.

- The establishment of pan-partnership pathways of care involving all relevant health and social care agencies, informed by patient and citizen needs, including rationalisation of acute/specialist provision where appropriate – for cancer and CV services in particular. The scale and connectivity that provides necessary patient volumes and concentration of clinical and academic expertise to underpin world-class performance would be challenging for an AHSC to achieve without mature links with the broader health community. We will replicate the evolving success of London Cancer, our integrated cancer care pathway for NC and NE London, for Cardiovascular Services, mental health and, over time, other major services.
- Drawing on the above capabilities and patient cohorts, we will acquire ‘real world data’ to inform research questions, e.g. the £14m TRACERx study of lung cancer where longitudinal and multi-tumour site sequencing to identify the level of intra-tumour heterogeneity will inform development of genetic biomarkers for personalised therapy. This approach will be extended to all Programmes.
- A secure framework for conducting clinical trials at scale with exemplary performance statistics in terms of recruitment, adoption and completion. Our associated Comprehensive Local Research Network (CLRN) hosts over 900 clinical trials including 170 commercial studies (over 25% of commercial studies in the National Institute for Health Research (NIHR) portfolio are led by Chief Investigators in UCLP). Harmonising procedures for gaining NHS permissions across all UCLP Trusts has transformed the setting up of trials, with the mean time for sign-off now just seven days for commercial studies. The CLRN is the highest non-commercial recruiter and the third highest commercial recruiter in the country, recruiting well over 40,000 patients a year. We will strive to be the exemplar site in terms of trial involvement, conduct and efficiency.

A second special feature of our AHSC partnership is that we represent an amalgam of specialist research institutes (e.g. at GOSH, Moorfields, National Hospital for Neurology and Neurosurgery), which have fostered remarkable success in focused areas reflected in the award of two BRCs, a BRC Programme and a BRU between them. We seek to build on that model embracing CV strengths at QMUL/Barts Health (CV BRU) and complementary infection expertise at LSHTM.

**How the success of the AHSC will be evaluated against specified objectives and deliverables:**

Fittingly, our success ultimately manifests as improved health outcomes and wealth generation. To that end, the following generic metrics will be captured and interrogated at Programme and AHSC Board level:

- **Health outcomes:** *Quality Improvement:* linked to the NHS Outcomes Framework and based on: clinical outcomes, Patient Reported Outcome Measures and Patient Reported Experience Measures. *Value Improvement:* cost-savings generated, increased delivery per pound invested; utilising resource-use proxies (e.g., number of repeat investigations, activity per full-time equivalent or session) where true bottom-up costing is not yet available.
- **Wealth outcomes:** Number of jobs created, number of patents granted, number of industry partnerships established, number of spin-outs, licensing deals, speed of research study approval, recruitment into research studies, number of trials, number of patients in trials. In addition to more traditional metrics, we will seek a more innovative approach to the measurement and evaluation of economic growth, drawing on our academic base and CASMI.
- To performance manage progress towards our research, clinical quality and education objectives, the following metrics will be collated across the partnership at Programme level:
  - Research: Number of Highly Cited Publications and PhDs, research grant/contract income.
  - Clinical quality: Adoption of a common clinical quality dashboard supported by a joint medical directors quality forum
  - Education: National Student Survey, National Training Survey, GMC Survey results, mandatory training, Employee Satisfaction Surveys

To reveal the effectiveness of our model of partnership, metrics will also be collected to reveal the added value from interdisciplinarity and inter-institutional engagement, including the number of joint grants, publications and trials.

To underline our commitment to leverage the talent of our workforce and views of our patient community, we will:

- Profile our AHSC workforce and seek to increase the number of women in leadership positions, and drive other facets of equality and diversity
- Survey consumer/citizen perspectives on engagement, service quality, and involvement in research, implementation and evaluation processes.

**Evidence that the partnership has a strong clinical informatics platform:**

Not only does UCLP regard a strong clinical informatics platform as the key enabler in pursuit of its purpose, but as a partnership seeks to play a leadership role in the establishment of advanced platforms for the broader benefit of the UK. To that end, we have identified informatics as a core underpinning initiative where
The collective talent possessed by the partnership ranging from computational science, computational modelling, handling and interrogation of large cohort data sets, bioinformatics, decision support tools, m- and e-health, preventative, diagnostic and therapeutic initiatives has been drawn together. This virtual community will have a physical focus in the newly established Farr Institute @ UCLP. This builds on the successful partnership bid from UCL, LSHTM, QMUL, Public Health England (PHE) and the Medical Research Council (MRC) Clinical Trials Unit to become one of the four centres in health informatics research. This provides the platform for an international centre of excellence in innovative health informatics research, which will maximise translational impact from discovery through trials to clinical practice, service delivery, patient outcomes and public health. Central to UCLP’s cross-cutting Informatics Programme, the Farr Institute @ UCLP has enabled closer links with the Wellcome Trust Sanger Institute, Francis Crick Institute, the European Bioinformatics Institute, and other centres of excellence, and we are presently awaiting the outcome of a major bid to extend this capability. Future opportunities to establish a regional hub for informatics capacity have emerged from this alliance, and at a national level, further funding has enabled collaboration across four Farr Institute centres (in Manchester, Scotland and Wales).

UCLP has established an Informatics Programme Sub-Board to align the clinical and research functionality of the platform and has appointed the Head of the Farr Institute of Health Informatics Research as Independent Chair. Relevant commercial links are being sought to facilitate data handling/synthesis at ‘industrial’ scale and a ‘safe data’ group, with patient and citizen representation, is actively involved to ensure confidentiality issues are addressed.

How will the partnership align NHS and university strategic objectives and increase translation?

Hospital and academic partners recognise that focus, critical mass of expertise and high volume patient flows in specialist areas are necessary if world class clinical and research translational performance is to be achieved. Specialist service provision is becoming increasingly concentrated in our part of London to meet those goals. The necessary strategic alignment between hospital Trust and academic partner is fostered by joint BRC/U activity in the relevant specialist area which contributes to all six of the AHSC’s Programmes. Each BRC/U has a joint Board involving Trust and University partner to co-develop strategy and ensure delivery. Examples of this successful alignment are exemplified by: the joint commitment of UCL and GOSH to create a new £87m Centre for Children’s Rare Disease Research with UCL securing Higher Education Funding Council for England (HEFCE) Research Partnership Investment Funding and aligned investment from the GOSH Children’s Charity; and, a successful bid to HEFCE for Catalyst funding to develop a presence at the Stevenage Bioscience Catalyst complemented by the successful bid to the UCLH/UCL BRC to fund ‘industry ready’ projects at the facility, reflecting a joint commitment to closer industrial engagement.

By increasingly considering our BRC/BRU activity as a portfolio, common metrics and shared best practice are further fostering strategic linkages. Dedicated research coordination support for the six AHSC work Programmes and underpinning cross-cutting initiatives in Informatics, Personalised Medicine and Lifelong Health create further alignment. The recently awarded CLAHRC has also galvanised strategic alignment and common purpose, bridging the translational gap between AHSC partnership and the broader AHSN constituency, and facilitating the later stages of translation, adoption and diffusion of research. For example, within the Eyes and Vision the CLARHC is co-designing a project with Moorfields to improve the pathway for people with chronic eye disease.

The AHSC governance arrangements are focused on securing strategic alignment between academia and the NHS, identifying and nullifying barriers to translation, and performance management of six core Programmes of activity. To that end the AHSC Planning and Performance Executive interrogates reports supported by appropriate metrics for education, care quality, research and wealth generation.

4. GOVERNANCE AND LEADERSHIP (2 pages plus an Organogram)

Detail the governance and leadership arrangements for the proposed AHSC including:

- Details of the organisational model and governance arrangements of the proposed AHSC. This should include an organogram outlining lines of accountability within the governance arrangements;
- Evidence of the functionality and effectiveness of the governance arrangements;
- A summary of how effectiveness of the governance arrangements of the partnership will be measured over the term of AHSC designation;
- Detail of the leadership of the proposed AHSC including key posts and post holders, illustrating how the posts will contribute to the delivery of the goals, visions and purpose of the proposed AHSC.
Organisational model and governance arrangements: Programme Steering Groups: Each of the AHSC Programmes will be led by an expert Steering Group. The Steering Groups will be responsible for the execution of the Programme strategy in accordance with the AHSC’s strategic aims and objectives as articulated by the AHSC Planning and Performance Executive.

The Programme Steering Group Chair will be responsible for galvanising the community, integrating an approach that embraces the potential of personalised medicine and lifelong health initiatives and the central role of informatics, reporting progress to the AHSC Planning and Performance Executive and facilitating integration with other AHSC Programmes and the wider AHSN. Chairs will have an exceptional track record of delivery and a breadth of experience across research, education and clinical care, and be supported by dedicated coordination expertise.

The Steering Group membership will involve relevant BRC/U and patient representation and expertise in discovery science, clinical trials, industrial engagement, wealth generation/enterprise/education and informatics with members drawn from appropriate institutions in the AHSC partnership.

Cross-cutting Sub-Boards: The AHSC’s cross-cutting Sub-Boards in Research, Care Quality, Wealth Generation, Informatics and Education underpin our Programmatic delivery. Each will be chaired by a world-leading expert in the field, and will bring together appropriate representatives from each of the AHSC Programme Steering Groups.

AHSC Planning and Performance Executive: The AHSC Planning and Performance Executive brings together the Chairs of the AHSC Programme Steering Groups and cross-cutting Sub-Boards. It is chaired by the UCLP Academic Director and is accountable to the AHSC Board.

AHSC Board: The AHSC Board takes constituent institutional accountability for ensuring that the AHSC fulfils its functions, approving strategy and assuring delivery of plans against specified objectives. Its membership will include the Trust Chief Executives and University Leads of the AHSC’s constituent organisations and the AHSC Academic Director, and will be chaired by UCLP’s Managing Director.

UCLP Chief Executives Group: The UCLP Chief Executives Group ensures the effective integration of the AHSC and AHSN activities by providing an engagement forum for the breadth of the integrated partnership. The membership includes all Chief Executives of the NHS Trusts and accountable university leads, and is chaired by the UCLP Managing Director. It ensures that the AHSC is properly informed by patient and population need and NHS priorities, and that institutional resources are deployed appropriately to support
Programmes of work proposed by the UCLP Board.

**UCLP Board:** The UCLP Board is chaired by the UCLP Chair, and acts as the custodian of UCLP’s values (to be patient-focused, transparent, collaborative and respectful), driving improvement in health and wealth outcomes through partnership working. The Board is responsible for approving and overseeing the delivery of UCLP’s integrated strategy across the AHSC and AHSN to improve health and wealth as well as the individual contribution of the two entities and that of our associated CLAHRC and CLRN. In particular it seeks to ensure that these constituent functions are increasingly aligned to optimise translation, adoption, diffusion and commercialisation. Membership of the Board includes the UCLP AHSC Academic Director, UCLP Managing Director and skills-based Non-Executive Director representatives from industry, local government and patient engagement, with the Chair of the local LETB in attendance.

**Evidence of the functionality and effectiveness of the governance arrangements:**

UCLP has established a governance arrangement that enables the broad engagement and buy-in of its partner organisations to effect change, whilst providing a robust accountability structure to manage performance and evaluate progress of the AHSC and other constituent functions.

- The **UCLP Research Sub-Board** has overseen the improvement in clinical trials performance, reconfiguration of the CLRN, development of the CLAHRC application and UCLP-Francis Crick Institute Informatics business case.
- The **Care Quality Sub-Board** (Medical Directors and Nursing Directors) has overseen an increasingly integrated and aligned approach to care quality management, including the production and implementation of quality metrics. The Nurse Directors’ achievements for 2012-13 include an elite, accelerated development Programme for newly qualified nurses to ward sister level; defining necessary attributes for managers across UCLP; developing tools to assess and stratify safety risk at ward/clinical level and to use this ‘heat-map’ to direct management attention and support. The Medical Directors have focused on emergency/urgent care and management of frailty, and the physical/mental health interface. The Care Quality Sub-Board also drives the quarterly UCLP Quality Forum, hosted since 2011 in rotation by different partner organisations (including Clinical Commissioning Group (CCGs), and providing a sharing/learning forum on cross-cutting elements of quality and safety.
- The **Education Sub-Board** oversaw the successful bid for an extensive portfolio of Postgraduate Medical and Dental Education Programmes, and supported the development of and transition to a LETB.
- The **Wealth Generation Sub-Board** is a new Sub-Board which will connect the Programme enterprise representatives and the leads of our partnership enterprise infrastructure to support commercial engagement, economic development and wealth creation. Its core objective is to bring together the combined capabilities of the partnership to share best practice and discuss opportunities for alignment and a joint approach. The Sub-Board will also connect with the pan-London ‘MedCity’ to co-ordinate and promote London’s Life Sciences contribution in which the AHSC is deeply involved.
- The **AHSC Planning and Performance Executive** is also a new body which is collectively accountable for setting and monitoring the delivery of the AHSC strategy through assessment and analysis of KPIs and appropriate performance management. It mirrors the highly successful UCL School of Life and Medical Sciences Planning and Performance Committee which fulfils identical roles across four Faculties and has driven an average 8% per annum increase in research income in the last four years.
- The **UCLP Chief Executives Group** has demonstrated its capacity to tackle challenging issues across the partnership through alignment of institutional objectives, joint sponsorship of work Programmes and rapid implementation; for example, i) recognising the value of peer review to drive clinical quality, e.g. the NHS Trust Medical Directors agreed to adopt a common approach to measuring and sharing information to improve standards, ii) recognising the centrality of nursing leadership to improve care and compassion, the promotion and support of the new ward sisters Programme to create leaders for the future (referred to above), iii) single sign-off for clinical trials consent, iv) service integration and rationalisation, v) sharing of best practice in relation to the rising tide of A&E admissions.
- The **UCLP Board**, as a custodian of UCLP values and the point of integration of AHSC and AHSN activities, has sustained a robust partnership culture over and above factional interests and negotiated complex service integration solutions (e.g. CV and cancer) in pursuit of the partnership’s purpose.

**How effectiveness of the governance arrangements will be measured:**

- Metrics that monitor deliverables defined by the stated Programme objectives of the AHSC
- Metrics that monitor the added value that derives from effective partnership working (i.e. the ‘more than the sum of the parts’ dimension) e.g. joint grants, publications and commercialisation
- Independent review of AHSC Board level governance arrangements and functionality complemented by Board member 360 degree feedback perspectives
Details of the leadership:

- **Academic Director** (Professor Sir John Tooke) will be accountable for defining and delivering the strategic priorities of the AHSC, leading partnership across the three universities, with national academic policy makers and with UK and global academic centres of excellence.

- **Managing Director** (Professor David Fish) supported by the **Chief Operating Officer** (Mr Julian Dixon) will be accountable for aligning the strategic priorities across research, education and clinical care, leading partnership working with NHS AHSC members, with national health policy makers, with the local AHSN and national network of AHSNs, and with global academic health systems.

- **Programme Steering Group Chairs:**
  - **Neuroscience:** Professor Alan Thompson, Dean UCL Faculty of Brain Sciences
  - **Child Health:** Professor Rosalind Smyth, Director, UCL Institute of Child Health
  - **Infection, Immunity and Inflammation:** Professor Hans Stauss, Director, UCL/Royal Free Centre for Immunity and Transplantation
  - **Cancer:** Professor Tariq Enver, Director, UCL Cancer Institute
  - **Cardiovascular:** Professor Mark Caulfield, Director Barts NIHR CV BRU
  - **Eyes and Vision:** Professor Sir Peng Tee Khaw, Director NIHR Specialist Biomedical Research Centre in Ophthalmology at Moorfields and UCL Institute of Ophthalmology

5. THEMES/WORK PROGRAMMES (4 pages per theme)

Please use the Specific Theme Form to complete this section (SpecificThemeForm_AHSC-2013-xxxxx). Please use a separate form for each of the six specific themes or work Programmes.
### UCL PARTNERS NEUROSCIENCE WORK PROGRAMME

#### 1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

<table>
<thead>
<tr>
<th>Name of the English NHS Provider/University Partnership:</th>
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<td>UCLPartners Academic Health Science Centre</td>
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#### 2. THEME / WORK PROGRAMME

##### 2.1 Name of the theme/work Programme.

**Neuroscience**

##### 2.2 Aims and objective of the theme/work Programme.

The neuroscience Programme brings together some of the world’s leading research groups in basic neuroscience, neurology, psychiatry and psychology creating novel interfaces where we believe much research progress can be made through an integrated approach. UCL is ranked first in Europe and second globally for research in neuroscience/behaviour and psychiatry/psychology, with research outputs being cited over a quarter of a million times in the past 10 years (Thomson ISI). UCL’s share of the world’s most highly cited papers in neuroscience is 23%, and the figure for neuroimaging is 27%. This Programme provides an ideal opportunity to bring together expertise and align resources to make a major therapeutic impact on neurodegenerative disease.

**Programme Aim:**

The over-arching aim of the Programme is that UCLPartners Academic Health Science Centre will become one of the leading centres in the world for the rapid development, application and evaluation of novel treatments and interventions for neurological, psychiatric and hearing disorders.

**Objectives:**

1. **Mental Health:**
   
   We will pursue initiatives that combine basic neuroscience, clinical and epidemiological psychiatry and clinical psychology to address the global challenges of mental health problems. We will apply basic neuroscience research to mental health disorders to explore the biological underpinning of these conditions. We will launch a new multi-disciplinary Institute of Mental Health in January 2014, which will be completed by December 2015 and will drive forward our research strategy. We will bring together the expertise to address the mental health burden of those with neurological illness and physical neurological health, allowing far better identification of co-morbidities such as anxiety and depression in patients with long-term neurological conditions, including early dementia/mild cognitive impairment, stroke and multiple sclerosis. For example, by 2014 we will initiate a trial to assess the use of psychological interventions to change behaviour and improve adherence to secondary prevention treatments and lifestyles in patients following stroke.

2. **Neurodegeneration:**
   
   By applying molecular, cellular, neuroimaging, epidemiological and cognitive approaches to neurodegenerative disorders affecting the brain, we will better define disease, illuminate mechanisms of pathogenesis and guide development of therapeutic interventions for disorders of the nervous system. We will design and validate a gene chip technology and protocol that enables the simultaneous sequencing of dementia genes, which will be a key tool in diagnosing genetic causes of dementia and assessing genetic influences across neurodegeneration. In dementia research we will build on: the generation and characterisation of induced pluripotent stem cells; the generation and collection of fibroblasts, upon which whole genome expression analysis will continue; and use cellular models of disease to screen for new therapeutics. We will open the Leonard Wolfson Experimental Neurology Centre (LWENC) in November 2013, which will provide a dedicated centre for first-in-man studies. In 2014 we will host the first clinical trial in symptomatic familial AD, with the LWENC as the only UK centre as part of the Dominantly Inherited Alzheimer Network (DIAN) trial. In 2014 we will launch a longitudinal imaging and biomarker study of the 1946 MRC birth cohort to identify both the earliest diagnostic features of Alzheimer’s disease and modifiable risk factors for cognitive decline. By January 2015 we will have launched first-in-man studies in Huntington’s Disease, Fronto-temporal dementia and prion disease. We will continue our ground-breaking work in prion disease, having developed a small molecule drug to block prion propagation (in collaboration with GSK) and completed the largest clinical trial to date in prion disease (PRION-1). We will re-provision the MRC Prion Unit into state-of-the-art facilities at the Courtauld Building, serving as an important resource for the interdisciplinary study of neurodegenerative disorders UCL-wide.
3. Neuroprotection:
Research focuses on multiple sclerosis (MS), studied in both in vitro and in vivo models, and including neuropathology, experimental medicine, neuroimaging and clinical trials. The research Programmes are cohesive, with some themes (e.g. tissue energy insufficiency) uniting the research of virtually all the members. The principal research goal will be to increase our understanding of the pathophysiology of MS and to develop novel therapeutic approaches for neuroprotection. We will further build on the partnership between UCL and QMUL to provide a hub of unparalleled trial capacity for MS, including evaluation of novel e-Health cognitive interventions as well as drug therapy. We will commence a multi-arm trial of three neuroprotective agents in progressive MS by January 2014 (MS Smart) and will launch a neuroprotective trial in early MS in conjunction with QMUL by October 2014.

4. Sensory systems and therapies:
We will bring together expertise in audition and cognition to transform understanding of the mechanisms underlying function and dysfunction in sensory systems. We will develop and validate new therapeutic approaches in areas ranging from stem cells to neuroprosthetics, and devices that provide novel interfaces between the real-world signals, prosthetic devices and the nervous system. Clinical trials will be undertaken to test and evaluate new and current treatments for ear, nose and throat problems, such as dizziness, hearing loss and sinus and ear infections, and we will translate the findings of studies into national and international evidence-based guidelines. We will establish a regenerative medicine network across the sensory systems in 2014 that will result in an intervention study involving inducible progenitor stem cells (iPSCs) by 2016, and will recruit researchers with expertise in iPSC technologies to seed a pipeline perspective for cell-based therapies in regenerative sensory therapies.

5. Understanding and influencing human behaviour:
We will exploit our expertise in behavioural and cognitive sciences, neurology and neuroscience to improve understanding of the basic neural and cognitive processes underlying human wellbeing, from infant development to aging, and to inform strategies for behavioural change interventions. We will establish an Institute for Behavioural Change by December 2013 which will lead on a number of interventional studies in 2014/2015.

6. Development of Neurological Biomarkers:
We will improve pre-symptomatic biomarkers to improve early diagnosis of disease. In collaboration with the LWENC, the dementia BRU has developed a cerebrospinal fluid (CSF) laboratory with new assays for neurodegeneration and we have validated two additional markers by 2015. The clinical service and research laboratory are closely linked allowing rapid translation; the CSF lab provides a dementia CSF analytic service to 20 hospitals in the South East. Our extensive patient cohorts that allow tracking of natural history will be utilised for biomarker discovery and validation. This will permit optimisation of methods for tracking the earliest manifestations of change in neurological diseases at a time when therapeutic intervention is most likely to be effective, and thereby help determine the feasibility and requirements of future, early phase studies.

2.3 Description of how the Programme will contribute to the aims of the AHSC.

**Partnership working:** Integral to the Programme are the links with the NIHR BRC and BRU, to support experimental medicine research and expedite the translation of basic science discoveries into therapies. The interface between the BRC and BRU, together with the LWENC, provides a novel setting for the conduct and engagement of experimental neurology with a diverse patient population and range of stakeholders across the partnership. The experimental neurology paradigms informed by the genomic support of the NIHR Bioresource will enable advances in stratified patient groups in: new therapies, including novel devices and first-in-man studies; improvements in diagnosis, treatment selection and evaluation of response; and repurposing of therapies. The Programme will also be part of the Dementia Translational Research Collaboration (TRC), which aims to pull discoveries from basic science into benefits for patients. In addition, within the BRC are national theme leads for neurodegeneration and neuromuscular diseases, in the NIHR Rare Diseases TRC. Currently, of the estimated 7,000 rare genomic disorders, in approximately 50% of these the genes are known, and many of the unknown disorders are either primarily neurological or have a very prominent neurological component to their phenotype. The National Hospital for Neurology and Neurosurgery at UCHL has an international reputation in rare neurological disorders and provides the ideal clinical base to make a major contribution.

**Industry Engagement:** We have demonstrated our ability to develop novel and exciting partnerships with industry, through our partnership with Eisai. This alliance will involve researchers from both organisations working together to investigate innovative ways of treating neurological diseases such as Alzheimer’s, Parkinson’s and other related disorders. The goal of the collaboration will be to identify and validate novel drug targets, develop new therapeutics and evaluate them in proof-of-concept clinical trials. This partnership arrangement provides UCL with access to an Eisai-owned compound library of 50,000 compounds (value £5million), for the screening of new targets. The establishment of this compound collection at UCL will provide significant benefit as it will enable the collaboration to utilise local UCL and Eisai expertise and capabilities to develop bespoke assays for the emerging novel targets. Other partnerships include GSK for the development of small molecule therapeutics for prion disease and with...
Lilly on imaging in dementia which has already led to a £1m in-kind contribution of amyloid imaging ligands. A range of approaches will be developed to engage with commercial life science organisations by building on current industrial partnerships, hosting industry showcase days; identifying how the world-class research of UCL and QMUL presents opportunities for industry; appointing business managers; and through engagement of UCL Enterprise and the Translational Research Office.

Informatics: We will leverage a number of existing bioinformatics initiatives, including the MRC HiRC-UK, NIHR BRC informatics initiative and MRC UK Dementias Research Platform, to play a leading national role in innovating the way data are linked, analysed and used to support research and service improvement for patients living well with dementia. In particular we will support delivery of two ‘next steps’ in the better research Programme of the Prime Minister’s Challenge on Dementia. The Programme will support roll out of the D-CRIS system which will enable the joining up of patient medical records in five mental health NHS trusts to facilitate research. The NIHR DeNDRoN Coordinating Centre team at UCL is leading on the development of a nation-wide, consent-for-approach list of people with dementia who agree to participate in research. The Programme will partner with the NIHR Clinical Research Network, Alzheimer’s Society and Alzheimer’s Research UK, acting as the ‘early adopter’ region for the implementation of the system in the NHS. The programme will engage with the Farr Institute @ UCLP to integrate complex data (e.g. ‘omic, imaging) to allow stratification of treatment response. In particular through the Dementia BRU we will shape the emerging Dendron registry, and explore its linkage to social care and neuroimaging data.

Global reach: The neuroscience Programme will link with other research organisations across the world to establish strategic alliances to benefit patients. In the field of MS, we play a leadership role in the Multiple Sclerosis International Federation, resulting in a global atlas of MS with the World Health Organisation (WHO), Quality Care Guidelines and a £20m collaboration to identify treatments for progressive MS.

The BRU has an international collaboration with the multi-centre Dominantly Inherited Alzheimer’s Network (DIAN) study where progress has been made in the use of imaging markers of early neurodegeneration in the at-risk cohorts, providing the world-wide image analysis for DIAN measurement of atrophy progression, a key outcome for clinical trials.

We have a productive research and training collaboration with the University of Zurich, with the aim of using our world-class strengths in this area to further understand and treat neurological diseases, and with the Max-Planck Society, with the establishment of the £6M Max Planck-UCL Centre for Computational Psychiatry and Ageing.

2.4 Description of how the Programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

Development of the workforce:
World-class education and training will be centred at UCL/QMUL and the Trusts. This will cover the provision of Academic Clinical Fellows and Clinical Lecturers training Programmes to develop the next generation of clinical academics, the provision of training and neuroscientific underpinning in key specialty areas, such as mental health, and the development of new postgraduate courses to address unmet needs in areas such as neurodegeneration and the sensory systems. For example, the Wolfson PhD Programme in neurodegeneration will develop a new cadre of basic and clinical researchers in this area, and we will work with UCL Enterprise to develop a new PhD Programme in Translational Science in the Sensory Systems. Partnership with the BRC/BRU will utilise opportunities for clinical research training through specific-funding streams.

Early-phase trials:
The opening of the LWENC will provide a dedicated resource for first-in-man studies of novel therapies for neurodegeneration and dementia that stem from our own fundamental science. Through close BRC and BRU Programme level engagement with the LWENC, we will use a combination of novel biomarkers, well-characterised at-risk cohorts, and sensitive and precise measures of progression to deliver proof-of-concept and first in-man studies at an earlier stage than ever before.

Public Engagement and Public-Patient Involvement:
We will embed PPI in all our research. This will include information sharing, where researchers describe the progress they are making in particular research projects, and receiving views on what patients want in terms of research priorities. PPI will contribute to the development of clinical studies, in steering the trial management group and in the dissemination of results. Dedicated PPI liaison officers will ensure that clinical trials will be developed with and by patients as full and equal partners. We will appoint dedicated leads for public engagement in specific areas such as MS, and host public open days to showcase our research. We will seek to develop ‘Citizen Reporter’ Programmes with members of the public interviewing UCLP scientists and clinicians, which will allow greater understanding and engagement around the area of neuroscience, and support dedicated social media interfaces.

Service users and carers:
We will promote a more systematic involvement of service users and carers in areas such as mental health treatment. We will develop systems of care through investing in effective befriending and patient-clinician communication. We will continue to develop and implement the collection of outcome metrics and patient
experience across pathways in areas such as stroke and multiple sclerosis. This exploitation of our informatics capabilities is a powerful integrative mechanism, such as the development of a patient-facing, web-based digital platform to allow MS patients to report outcomes and to support self-management. One exemplar at the National Hospital for Neurology and Neurosurgery is NeuroResponse, a nursing-led platform to provide telephone, email and video based advice for both patients and local clinical care teams to support patients with MS. This has resulted in a 30% reduction in A&E visits for this population.

2.5 Description of how the Programme will involve and enhance multi-disciplinary and multi-professional working.

Our capacity to harness multidisciplinary perspectives underpinned our success in the award of the LWCCN and the Sainsbury Wellcome Centre for Neural Circuits and Behaviour, facilitated by our pan-faculty neuroscience domain and dedicated research coordinator support. We will build on that success to promote multi-disciplinary and multi-professional working through clear communication between the leads for specific neurological areas and aligning the support provided by the UCL Neuroscience Coordinator, UCLP, BRCs, Dementia BRU and CLRN. The BRC neuroscience Programme is an exemplar of multidisciplinarity, involving imaging, biomarkers and clinical phenotyping to maximise the usefulness of data already being collected by the NHS. We will demonstrate commitment to the whole force through multi-professional Programmes of research training.

A joint UCL/OMUL strategic initiative working across neuroscience, CV and mental health Programmes will be developed to support a major academic translational development in the area of cerebrovascular disease, supported by the BRC. It will facilitate recruitment of world leaders in stroke research and clinical trials working in the fields of ischaemia and neuroprotection. We will look to develop models capable of providing an easily interpretable ‘physiological fingerprint’ of brain status through work on cerebral haemodynamics to identify cerebral ischaemia, and to allow translation of novel treatments which can then be rapidly applied to the successful clinical stroke pathways designed by UCLP. The initiative will also facilitate a planned multi-disciplinary project to improve the early diagnosis of cognitive impairment after TIA and stroke and delay the onset of dementia by aggressive treatment of CV risk factors across large patient populations, harnessing a wide range of resources and ensuring rapid, extensive application.

The Programme will work closely with the Eyes and Vision Programme to exploit commonalities to drive forward a therapeutic agenda in sensory systems, linking two world-class Institutes (the Ear Institute and the Institute of Ophthalmology). Research will focus on patient-centred stem cell therapy and sense organ regeneration involving UCL and QMUL and on transforming existing approaches to prosthetics that interface with the central nervous system, combining engineering solutions with cell, gene or small molecule therapy designed to optimise the fit of the device to the brain or spinal cord.

Division 1 of the CLRN, led by Professor Alan Thompson, includes Dendron, Ophthalmology, Stroke, CV and Neurological Disorders. This provides significant opportunities to pool resources to increase the number of clinical trials across Central and East London, increase patient recruitment and explore patient experience that will be common across the related disease areas. We will develop a joint Programme of disease prevention in avoidable morbidity, which will encompass multiple areas. Focusing on early diagnosis, shared risk factors and on behavioural change and health educational strategies, the Programme will link the Behaviour Change Unit at UCL, the Wolfson Institute of Preventive Medicine at QMUL, and the expertise in epidemiology and Public Health in UCL and QMUL.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work Programme.

The neuroscience Programme will be led by an expert Steering Group of representatives drawn from across the UCLP partnership. The Steering Group will be responsible for the delivery of the neuroscience strategy, and in accordance with the AHSC’s strategic aims and objectives. The membership will incorporate appropriate discovery, clinical, applied, evaluation, education and enterprise expertise, and will include a patient representative. The Programme Steering Group Chair (Professor Alan Thompson) will be responsible for integrating the community in the Eyes and Vision strategy and reporting progress (including agreed metrics) to the AHSC Planning and Performance Executive (as outlined in section 4). The key individuals responsible for leading the neuroscience Programme are:

- **The key individuals and organisational contributors responsible for delivering the Child Health theme** are UCLP, UCLH/UCL BRC, Dementia BRU, UCL, QMUL, GOSH/ICH, the Francis Crick Institute
- **Mental Health:** Peter Fonagy, Michael King, Gill Livingston, Elvira Bramon, Geraint Rees, Ray Dolan
- **Neurodegeneration:** Martin Rossor, Nick Wood, Nick Fox, Sarah Tabrizi, Tony Shapira, John Collinge, Mike Hanna
- **Neuroprotection:** Ken Smith, Olga Ciccarelli, Gavin Giovanni, David Baker, Charlie Davie, Jeremy Chataway
- **Sensory Systems:** David McAlpine, Martin Birchall, Anne Schilder, Jonathan Gale
- **Behaviour Change:** David Shanks, Susan Michie, Gabriella Vigliocco
- **Biomarkers:** John Hardy, Henrik Zettenberg, Simon Heales, Jon Rohrer

Application Ref: AHSC–2013-10018
UCL PARTNERS CHILD HEALTH PROGRAMME

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership:
UCLP Academic Health Science Centre

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work Programme.
Child Health

2.2 Aims and objective of the theme/work Programme.
Programme aim: We will improve the health of children and the adults they will become, by conducting world-class research to translate discoveries about the aetiology of disease into better strategies for prevention, diagnosis and treatment. Through excellent educational Programmes we will disseminate and implement all relevant research findings to achieve better outcomes in childhood and throughout the life-course. We will also translate findings from population and clinical research (for example around possible gene/environment interactions) to inform basic research into mechanisms of disease.

Promoting the health of children lays the foundation for good health throughout life. Treatments have transformed illnesses, once fatal in childhood, to chronic conditions, but for many of them the aetiology is unclear and therapies suboptimal. This Programme is built on the close partnership between GOSH and ICH, UCL, which together form the largest grouping of biomedical research dedicated to children, outside North America. The unique and diverse patient cohorts, at GOSH, provide an exceptional resource to improve understanding of rare diseases and to translate findings quickly and efficiently into patient benefit.

We will leverage this through the outstanding, multidisciplinary expertise of the NIHR GOSH BRC and the planned Centre for Children’s Rare Disease Research (CCRDR), an £80m investment by GOSH, GOSH Children’s Charity and ICH. This integrates with UCLP’s sponsorship of rare disease research, within the Global Medical Excellence Cluster (GMEC) framework.

Our work is focussed on the six areas below – and ICH and GOSH are developing a joint research strategy, based on these areas, which will align with the GOSH BRC themes:

1. Genetics and Genomic Medicine: Building on the activities of the BRC-funded Centre for Translational Genomics (GOSgene), utilising advances in 'omic technologies (genomics, proteomics, metabolomics), together with deep phenotyping, we will develop biomarkers, diagnostic tests and specific and personalised therapies. Deliverables will be to set-up a “genome clinic” at GOSH to utilise personal sequence data and develop strategies that inform therapeutic decisions (stratified medicine) and life-style interventions where necessary; to work with the Farr Institute @ UCLP to develop tools to integrate electronic health records with genome data. We will initiate a clinical exome diagnostic service to enable sequencing of all children, with a clearly defined phenotype, who do not, on their second visit to the hospital, have a genetic diagnosis and extend this to full genome sequencing to translate these discoveries into identification of “at risk patients” and the development of specific treatments, for example through gene and cell-based therapies.

2. Developmental Biology and Cancer: addresses birth defects and childhood cancers, to inform development of novel preventive and treatment strategies, including stem cell therapies and regenerative medicine. Our new Birth Defects Research Centre will provide an international focus for congenital disorders research. We will undertake a pan-Europe clinical trial, which has resulted from our preclinical research, of a novel preventive therapy for spina bifida, alongside folic acid. We will use stem cell isolation and manipulation to generate desired cell types for in vivo use, prior to taking stem cell transplantation into new clinical areas; for example, for retinal repair in congenital photoreceptor degeneration, with Eyes and Vision. We will refine tissue-engineering approaches to ‘autologous’ organ regeneration and repair in the oesophagus and other organs, as already undertaken for tracheal stenosis. With the Cancer Programme, we will develop sensitive assays for detection of minimal residual disease in leukaemia, and new biomarkers for more accurate stratification of cancer patients. Trials will start of new therapies specific for proteins that play key roles in driving growth of leukaemias and Wilms’s tumour. Immunotherapeutic approaches for neuroblastoma and medulloblastomas will be evaluated, and we will open a dendritic cell vaccine trial for high-grade glioma.

3. Developmental Neurosciences: works closely with the Neuroscience Programme and integrates the clinical delivery of designated National Specialised Commissioning Team services for epilepsy and neuromuscular diseases, the highly specialised tertiary services for neurocognitive and mental health disorders with excellence in electrophysiology, neuroimaging and neuropathology. We will develop novel therapeutic interventions for epilepsy, based on knowledge of specific cellular and metabolic pathways (e.g.
neuroprotective therapies and ketogenic diet) and using genetics (pharmacogenomics) and imaging (EEG-fMRI) to stratify patients for clinical trials. With the MRC Neuromuscular Centre (linking London and Newcastle) we will continue to develop mutation-specific, novel, genetic therapies, using antisense oligonucleotides, and bring these novel therapies to a number of rare neuromuscular disorders for which no treatment option is available so far.

4. Infection, Immunity and Inflammation (III): integrates with the III Programme of UCLP and with comprehensive specialist clinical services at GOSH; the latter include state-of-the-art molecular diagnostics and therapeutics (e.g. antibody replacement, thymus transplantation, NCG-funded haematopoietic stem cell transplantation and gene therapy, and application of novel biologics). We are a world-leading centre for first into man cell and gene therapy studies in immunohaematological disease and the lead organisation for several international collaborative trials; we have developed a robust on-site infrastructure for manufacture of Advanced Therapy Medicinal Products to Good Manufacturing Practice standards, which will be further expanded in CCRDR. We will establish complex gene and cell therapies as standards of care for Severe combined immunodeficiency (SCID) and immunodeficiencies including Wiskott-Aldrich Syndrome and Chronic Granulomatous Disease and expand this to other paediatric infectious diseases such as Haemophagocytic lymphohistiocytosis and X-linked lymphoproliferative disease, and disorders such as those affecting the skin (Netherton’s Syndrome and Epidermolysis Bullosa). We will collaborate with industrial partners to deliver new therapies for patients with adrenoleukodystrophy and haemoglobinopathy. We will evaluate newborn screening for SCID in the UK and explore potential for screening of other severe immune disorders, for which early interventions predict excellent long-term outcome. With UCLP, we will continue to develop our expertise in manufacture of T cell therapeutics focussing initially on defined tumour antigens (e.g. WT1, CD19 for B cell malignancies) and viral infections (e.g. CMV, Hepatitis B). We will lead the first ever trial of biologics in childhood polyarteritis nodosa, the MYPAN trial, and be a leading centre in the world’s first randomised controlled trial (RCT) of Juvenile idiopathic arthritis -associated uveitis (SYCAMORE trial), to test efficacy of Adalimumab. Our longer-term deliverables will be to use the new facilities at CCRDR and the infrastructure of UCLP to expand cell and gene therapies to a much wider range of inherited (haematologic and metabolic) and acquired (infectious disease and cancer) disease, with integration into care pathways. Industry partnerships will facilitate the adoption of these agents as licensed medicines, and the dissemination of effective therapies globally.

5. Cardiovascular: With the CV Programme, we will take advantage of patient cohorts, e.g. congenital heart disease and cardiomyopathies, and specialist services, e.g. for paediatric transplant, pulmonary hypertension, bridge to transplant, neonatal and paediatric extra corporeal membrane oxygenation to translate novel patient-specific treatment options into safe care pathways of international relevance. We will use our techniques of integrative computer modelling of congenital cardiac defects to construct personalised devices such as mitral and aortic valves for percutaneous implantation thus avoiding surgery and its associated morbidity.

6. Population Policy and Practice: GOSH/ICH is unique among leading child health centres in being world leading in both basic sciences and population health sciences, and we will realise this cross-disciplinary research potential. With the MRC Centre of Epidemiology for Child Health, we will use unique patient cohorts and lifecourse methodologies to study the interaction between genetic and environmental factors and their impact on disease onset and progression to improve long-term outcomes.

2.3 Description of how the proposed theme or work Programme will contribute to AHSC aims.

Global Reach: We have recently visited world-leading children’s academic medical centres, to inform our strategy and to forge strategic alliances. We will formalise existing collaborations into exchange Programmes for clinical, PhD and postdoctoral scientists and develop broad international consortia around rare diseases research, building on mutual interests and our unique strengths in rare diseases research, which combine basic, clinical and population sciences. Specifically, new Programmes or strengthened links are underway with SickKid’s Hospital, Toronto, Children’s Hospital of Philadelphia and Cincinnati Children’s Hospital.

Partnering working: The focus on rare diseases within GOSH/ICH offers a unique potential to improve outcomes for the 3.5 million people in the UK who have a rare disease, most of which start in childhood. This has the potential to transform diagnosis through integrative deeper phenotyping combined with next generation sequencing and multi-omics datasets. For example, the GOSH/ICH BRC has funded the “HIGH5” Childhood Rare Diseases Programme to combine whole genome next generation sequencing with endo-phenotypes (from transcriptomic, proteomic, metabolomic and epigenetic characterisation of individuals) for five rare childhood-onset diseases which will map onto clinical data. UCLP will provide integrated care pathways for interpretation of actionable findings for children and families and work with Genomics England to deliver whole genome sequencing of 100,000 people with rare disease and cancer. Recently, with NIHR funding, we have developed a new approach using cell-free fetal DNA circulating in maternal plasma and molecular karyotyping for fetal sex determination and Down syndrome for diagnostic testing through the NHS Regional Genetics Lab (based at GOSH). Over the next four years UCLP will evaluate the role of these tests in clinical practice and expand this approach to multiple syndromic single gene disorders.
We will build on the over 25 multicentre collaborations led by GOSH/UCL, including: MCADD Screening Programme (Dezateux), Wiskott-Aldrich syndrome (Thrasher), Surveillance study of congenital adrenal hyperplasia, UK Collaborative Study of Congenital Heart Defects, North Star Network for neuromuscular diseases (Muntoni), Septo-Optic dysplasia (Dattani), National Congenital Rubella Surveillance Programme (Tookey). GOSH nephrologists (Bockenhauer, van’t Hoff, Marks, Waters) have key roles in the Renal Association Rare Disease Programme, with international collaborations (e.g. European Network for the Study of Ophan Nephropathies). GOSH hosts the Co-Director for the NIHR Medicines for Children Research Network (MCRN) and recruits well to MCRN studies.

**Industrial engagement and collaborations around child health:** Through the BRC, we have a dialogue with pharmaceutical and biotech companies which focus on rare diseases to address their requirements for early and late phase clinical research. There are currently more than 47 active industrial partnerships with 30 different companies in place at GOSH/ICH, and we plan to build on these to develop many more. These range from therapeutic trials for rare forms of epilepsy and Duchenne Muscular Dystrophy to the development of a new device for scaphocephaly/craniosynostosis. Examples are listed here:

<table>
<thead>
<tr>
<th>Mucopolysaccharidoses</th>
<th>Dr. Ashok Vellodi</th>
<th>Genzyme &amp; Shire</th>
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<tr>
<td>Cryopyrin Associated Periodic Syndromes</td>
<td>Dr. Paul Brogan</td>
<td>Novartis Pharma</td>
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<tr>
<td>Metastatic rhabdomyosarcoma</td>
<td>Dr. John Anderson</td>
<td>Hoffma, nn-La Roche Inc</td>
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<td>Lennox-Gastaut Syndrome</td>
<td>Prof Helen Cross</td>
<td>Eisai</td>
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<tr>
<td>Duchenne Muscular Dystrophy</td>
<td>Prof Francesco Muntoni</td>
<td>GSK, PTC and Sarepta, Summit, Prosensa</td>
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<tr>
<td>Mitochondrial mutation test</td>
<td>Prof Maria Bitner-GLindzicz</td>
<td>DIASOLVE, Pfizer</td>
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**2.4 Description of how the work Programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.**

**Informatics:** UCLP hosts a new MRC EHIRC and with the new national Farr Institute @ UCLP, with its maternal child health research theme, will develop the eMedLab initiative to integrate genomic data with health records from children. The generation of integrated high-quality child-health related datasets will enable development of a bioinformatics framework to test hypotheses, understand disease mechanisms, and identify health-related solutions.

**Public Engagement and Public-Patient Involvement:**
We are fully committed to involving children and families as equal partners. GOSH/UCL staff is actively engaged with over 100 patient organisations to support families, work collaboratively to engage potential participants and share the burden of research for them (e.g. Medical Protection Society support for Enzyme trials). We join with patients (Beales, Ciliodopathy Alliance, van’t Hoff, cystinosis) and patient groups (Kinsler, congenital melanocytic naevus) as research co-investigators. We work closely with groups such as Genetic Alliance to support Rare Disease awareness.

**Education:** We will continue to develop our unique, nationally-relevant child health educational Programme at ICH, with specialist input from clinicians at GOSH and other UCLP members. This currently offers a comprehensive and growing suite of courses in Child Health for undergraduates and postgraduates, which support career development for a range of health professionals. We will develop Programmes that respond to the changing needs of the NHS and other healthcare systems and which provide training to healthcare professionals to enhance their professional competencies and employability. Our portfolio of continuing professional development courses will address the requirements of specialist societies and Royal Colleges and we will expand this to cover more paediatric specialties and rare diseases. We offer over 60 short courses per annum to a wide range of health care professionals interested in child health. Numbers are increasing rapidly and we are looking to expand capacity in postgraduate education in child health, by offering new Programmes, such as a new MSc in rare diseases research.

**Research capacity development and talent management:** Research-led teaching is an important element of ICH and UCL academic strategy; currently we offer an MSc in Cell And Gene Therapy and an MRes in Biomedicine; we plan a number of further MSc degrees at the basic/translational interface and the first MRes in Child Health in the UK. These Programmes provide a springboard for students to undertake a PhD in child health. ICH has an outstanding PhD Programme, covering a broad spectrum of child health topics, ranging from basic, through clinical to population sciences and 93% of full-time students now submit within four years. We will expand this, particularly in clinical and population sciences and the training provided will be supported by ICH’s underpinning principle of “developing academic leaders”, with UCL’s Academic Careers Office. We also run the largest postgraduate clinical academic training Programme in the UK with a total of 22 Academic Clinical Fellows and 10 Academic Clinical Lecturer posts currently running at ICH/GOSH. We will expand and develop the excellent, integrated training provided for early career academic staff in clinical and non-clinical disciplines and, through partnership with other UK academic and NHS organisations, ensure that our trainees enhance the quality of child health research, clinical care and teaching throughout the UK, by actively promoting them to take up positions across the UK.
2.5 Description of how the theme/work Programme will involve and enhance multi-disciplinary and multi-professional working.

**Cross-disciplinary research:** Through integration of the Population Policy and Practice theme with our other themes, we will exploit our unrivalled opportunity to develop an ambitious cross-disciplinary research approach, to, for example, align developmental phenotypes alongside complex genomics, epigenetics, with the exposome, and bioinformatics and health informatics including the electronic patient record.

**Multidisciplinary care for children’s rare diseases:** Of the 70 Nationally Commissioned Highly Specialised Services, GOSH hosts/partners in 21 (UCLP 31); an important part of our strategy is to work with regional referral centres to improve clinical management of these patients throughout the UK. Delivery of care to children with rare diseases requires co-ordinated multidisciplinary approaches and we will use the insights we gain from understanding mechanisms of disease to refine this further. For example, the Dubowitz Neuromuscular Centre provides a multidisciplinary service (national designation in 2000) for the assessment, diagnosis, treatment and rehabilitation of children with Congenital Muscular Dystrophies and Congenital Myopathies which is fully integrated with research into disease mechanisms and novel therapeutics. Adolescents then transfer to the adult service within UCLP through a successful shared-care model to ensure continuity into adulthood. A rare disease service was designated in 2010 for the Bardet-Biedl syndrome. Multidisciplinary clinics are held in four trusts in Birmingham and London. The same "one-stop shop" model involving seven clinical specialists is applied at all four centres ensuring all affected children have the same excellent standard of care. The specialist service works closely to support primary and secondary care by providing bespoke care plans and educational advice on this rare condition. Other specialist services such as assessment of gut motility disorders and bladder extrophy management provide indispensable models of care for children with rare, hard-to-manage problems.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work Programme.

The Child Health Programme will be led by an expert Steering Group of representatives drawn from across the UCLP partnership. This will include the leadership team for our existing NIHR GOSH BRC. The Steering Group will be responsible for the delivery of the Child Health strategy, and its accordance with the AHSC’s strategic aims and objectives. The membership will incorporate appropriate discovery, clinical, applied, evaluation, education and enterprise expertise, and will include a patient representative.

The Programme Steering Group Chair (Professor Rosalind Smyth) will be responsible for integrating the community in the Child Health strategy and reporting progress (including agreed metrics) to the AHSC Planning and Performance Executive (as outlined in section 4). The Chair has an exceptional track record of delivery and a breadth of experience across research, education and clinical care, and will be supported by dedicated coordination expertise.

The key individuals and organisational contributors responsible for delivering the Child Health theme are UCLP, UCL ICH, GOSH, NIHR GOSH BRC:

**Genes and Genomic Medicine:** Phil Beales, Gundrun Moore, Maria Bittner-Glindzicz, Mehul Dattani, John Achermann

**Developmental Biology and Cancer:** Andrew Copp, Kathy-Pritchard-Jones, John Ham, John Anderson, Jane Sowden, Paolo di Coppi.

**Developmental Neurosciences:** Francesco Muntoni, Jenny Morgan, Helen Cross, Faraneh Vargha-Khadem, David Skuse

**Infection, Immunity and Inflammation (II):** Adrian Thrasher, Bobby Gaspar, David Goldblatt, Lucy Wedderburn, Persis Amrolia, Tessa Crompton, Christine Kinnon Thrasher

**Cardiovascular:** Andrew Taylor, Perry Elliott, CLRN

**Population Policy and Practice:** Catherine Law, Carole Dezateux, Russell Viner, Terence Stephenson, Jugnoo Rahi.
1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership:
UCL Partners Academic Health Science Centre

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work Programme.
Infection, Immunity and Inflammation (III)

2.2 Aims and objective of the theme/work Programme.

**Aim:** The goal of the III Programme is to transfer novel concepts in infection, immunity and inflammation research into new diagnostic tools and therapeutic interventions for the local and global patient population. Multidisciplinary research and training Programs serve to educate the next generation of scientists and health professionals. Joint working with industry will accelerate the implementation of novel therapies as routine treatment. Partnership working between Healthcare Environment Inspectorates (HEIs) and NHS Trusts is key to the development of the Institute of Immunity & Transplantation (IIT) and the Bloomsbury Research Institute (BRI), two UCLP-facilitated strategic initiatives to create world-leading centres for translational science.

**Objectives:** We will bring together researchers, clinicians, nurses, patients and regulatory experts to achieve the following four objectives: 1) develop novel immune interventions to treat disease; 2) improve the prevention and control of infection; 3) implement new therapies for inflammatory conditions; 4) establish next generation diagnostics underpinning personalised medicine.

**1. Novel immune interventions:** We aim to develop novel immune-enhancing interventions for the treatment of cancer and infection and tolerance-inducing strategies to treat autoimmunity and enable long-term benefits of conventional and bioengineered tissue/organ transplants. We will apply UCLP’s expertise in the development and clinical testing of vaccines, antibody, cell and gene therapy to achieve diseasetailored immune modulation.

**Infection:** with cytomegalovirus causes substantial morbidity in immune compromised patients. We will extend our recent trial results (Lancet 2011, 377:1256) and develop a set of immune intervention strategies to prevent CMV disease and complete the following clinical trials within the next 3 years: i) an industry-sponsored trial (Genentech) to test anti-CMV antibody products in transplant patients; ii) working with Cell Medica, a small to medium enterprise (SME) we will deliver the first randomised phase III anti-CMV T cell therapy trial to facilitate the commercial development of T cell therapy; iii) deliver phase I/II trial to test whether T cell receptor gene therapy can restore viral immunity in patients. Similar immunotherapy approaches will be developed for Epstein Barr Virus and Hepatitis B Virus.

**Cancer:** UCLP researchers have been instrumental in defining the immune regulatory functions of the CTLA4 and PD1 molecules. Recent studies showed antibody blockade of these molecules in therapy-resistant melanoma and lung cancer resulted in lasting benefit in 10-30% of patients. With commercial partners, in 3 years we will complete trials assessing the efficacy of CTLA4 and PD1 blockade as single and combination therapy in renal and lung cancer.

UCLP academics are at the forefront of developing immunotherapy with T cells engineered to express cancer-specific T cell receptors (TCR) or chimeric antigen receptors (CAR), and we were first in Europe to use TCR gene therapy in leukaemia and solid cancers.

**Autoimmunity:** Our discovery that severe infantile onset inflammatory bowel disease (IBD) is an inherited autoimmune disease caused by mutations in IL10 or IL10R genes led to treatment with hematopoietic stem cell transplantation which was found to be curative (NEJM 2009, 361:2033; JACI 2013, 131:825). However, it is unlikely that single gene defects account for later onset IBD. Hence, we will use well-characterised IBD cohorts and aim to combine next generation sequencing, new bioinformatics tools and functional analysis to uncover IBD susceptibility genes and pathways. We aim to improve IBD diagnostics in the next 2 years and test new biological interventions in clinical trials within the next 4 years.

We have extensive experience dissecting immunological mechanisms of type 1 diabetes in experimental...
models and in humans. We will combine genetic analysis of type 1 diabetes patients with detailed immune function tests to identify disease-causing pathways as targets for new therapeutic tolerance-inducing interventions which will be tested in clinical trials in the next 5 years.

**Regenerative medicine:** Over the last five years, UCL regenerative medicine groups received £75m of grant income and led more clinical trials than any other centre in Europe. This research strength, combined with the translational capability of UCLP, led to the clinical delivery of the first in human regenerative medicine trachea replacement and in 2013 to the award of a £2m UK Technology and Strategy Board grant to further validate this technology in patients. The UCLP regenerative medicine and immunology groups will work together to define the nature of the immune responses against artificial tissues and biomaterials, and develop interventions to prevent rejection. Our membership of the UK Regenerative Medicine Immunology network will facilitate this work.

2. **Infections:** The major challenge in tackling emerging infections is the widespread and varied nature of the threat. The UCLP solution is to combine the expertise of UCL and the London School of Hygiene and Tropical Medicine to jointly develop the Bloomsbury Research Institute as Europe’s largest groupings of infection-related researchers. The BRI will integrate excellence in pathogen biology with expertise in human immunology and genetics, mathematical modeling, population biology, clinical sciences and public health policy to develop tools to predict, map, and overcome newly emerging infections, and those representing new forms of existing infections, for instance drug and vaccine resistant strains.

**Early warning indicators** will decrease the burden of persistent infections, ensure earlier presentation and consequently reduce disease morbidity, mortality, transmission and emergence of antimicrobial drug resistance. Through development of early warning indicators of infectious disease, involving novel nanotechnology-based point of care tests through to use of social networking, we will: (i) reduce healthcare associated infections, through more rapid detection of *Clostridium difficile* and methicillin resistant *Staphylococcus aureus* (MRSA), and Gram positive bacteria, issues of great concern to our NHS Hospital partners; (ii) enable more rapid detection of newly emerging epidemic/pandemic strains of influenza; (iii) develop and implement point of care HIV testing in the UK and developing world. This is underpinned by a £14m grant from the EPSRC, and strong links with PHE. Google and others.

**Genomic science** was recently applied by UCLP researchers to track the animal origin and hospital spread of Middle East respiratory syndrome coronavirus outbreaks (NEJM 2013 369:407). We will build on our worldwide strength in the molecular epidemiology of pathogen spread, to build core genomic science into state-of-the-art PHE surveillance structures, to map and intervene in new outbreaks within our population. Individualised treatment regimens will be facilitated by integrating pathogen sequencing into routine diagnostic protocols, enabling rapid detection of drug resistance mutations. With our unique Programme of work developing early warning systems for infectious diseases and genomics (UCL, LSHTM, QMUL, Sanger Centre, 100,000 genomes project), which involves collaboration with PHE, we will radically alter the local and national delivery of information for clinical and public health action.

**Host/pathogen interactions as therapeutic targets:** Our most recent studies have revealed novel molecular host/pathogen interactions controlling HIV infection in humans (Nature 2013 in press). We aim to exploit the previously identified tripartite motif (TRIM) family restriction factors and perform in the next 3 years phase I/II gene therapy trials to explore whether TRIM-cyclophilin fusion proteins can protect against HIV infection in patients.

**New drugs to overcome antibiotics resistance:** Applying a focused and concerted approach to produce a new range of validated antimicrobials using the multidisciplinary platform encompassed in the UCLP infection Programme, a central vision is to develop world-leading target identification in the field of antibiotics. Three strategies towards novel antimicrobial design will be employed – (i) traditional kill, (ii) anti-virulence and (iii) novel non-chemical approach – that will provide a unique portfolio of validated antimicrobials based on our research synergy.

3. **Inflammatory Conditions:** We plan to extend our leadership in the development of biomarkers, biologic therapies and drug discovery. We will focus on amyloidosis, scleroderma and RA to take advantage of our academic and clinical leadership in these conditions.

**Antibody and drug treatment of amyloidosis:** Academics at the UCL Wolfson Drug Discovery Unit and NHS National Amyloidosis Centre have developed a collaborative clinical Program with GSK to produce a unique small molecule and humanised monoclonal antibody combination for treatment of all types of systemic amyloidosis, aiming for first patient studies in early 2013/14. The discovery in preclinical tests that depletion of serum amyloid P component can enhance the immune response to DNA vaccination will be tested in clinical trials with an HIV vaccine over the next 3 years.

**Novel treatment of scleroderma:** The research strategy in scleroderma exemplifies the principles of translational research by harnessing data from fundamental studies of disease biology including novel mouse models and moving via *in vitro* studies of explants and biopsy material towards novel clinical trials. UCLP clinical academics led the UK studies of anti-TGF-β1 biological therapies in scleroderma. Our recent studies of the role of IL-6 in scleroderma underpin an international trial of anti-IL6, sponsored by Genentech-Roche. We anticipate that UCLP will be the major recruiting centre for this trial.

**Biological therapy of RA:** Building on our pioneering use of biologic therapies for RA, our goal of
harnessing the immune system to restore tolerance in RA will focus on identifying cellular mechanisms of activity and correlates of responsiveness to therapy. We will develop an intensive biomarker Programme to establish profiles that will personalise which biologic therapy for inflammatory arthritis.

4. Diagnostics underpinning personalised medicine: We will bring together the world-class clinical science and informatics expertise of the partners to drive the next generation diagnostics based on the effective integration of genetic, functional and clinical data Linking deep sequencing to deep phenotyping: The NIHR-BRIDGE Programme will generate extensive exome sequencing data of our patients with immunodeficiency. We will perform extensive phenotypic and functional analyses of patients’ immune cell subsets and link phenotypic and functional abnormalities to the identified genetic defects.

Integration of clinical and research databases: Linkage of national infection data to electronic health records together with novel statistical approaches will create a central information resource that can be utilised to understand the epidemiology and control of infectious threats e.g. influenza, tuberculosis and HIV, and the effectiveness of public health interventions. This will allow us to understand the infective causes of chronic diseases, and which infections act as triggers for cancer, CV or neurological diseases.

Gene arrays and next generation sequencing for genetic diagnostics: The transfer of these technologies from the research labs to an accredited diagnostic lab will be facilitated by joint working between academics and biomedical/clinical scientists and the co-location of the laboratory facilities. We anticipate that within 2 years we will establish fully accredited gene array diagnostics for a number of inherited conditions. Joint working with commercial diagnostic providers will facilitate dissemination of the new diagnostic tests.

2.3 Description of how work Programme will contribute to the aims of the AHSC.

Partnership working: Investment in new infrastructure joining clinical and research activities via multidisciplinary research teams and across multiple clinical specialties has enabled the creation of the Institute of Immunity and Transplantation (IIT) and the Bloomsbury Research Institute (BRI). The IIT, was founded in 2013 and has leveraged £33M capital investment from UKRPIF and not-for-profit donors. The BRI is a partnership between the London School of Hygiene and Tropical Medicine and UCL to create a centre of research excellence in infectious diseases. Leading translational science: Underpinned by strong infection, immunity and inflammation research, we will deliver a spectrum of first in man phase I/II trials to test research findings in patients. We will further improve our infrastructure and know-how to deliver complex biological therapies in clinical settings and use comprehensive genetic, functional and phenotypic data integration for patient stratification. We have established strong links with the Francis Crick Institute (see key investigators in 2.6) and will develop exchange programmes for scientists and clinicians to provide UCLP researchers with cutting edge research training, and Crick researchers with access to patient samples and trial infrastructure. Industry engagement: Accelerated progression of industry-ready UCLP projects will capitalise on a unique opportunity offered by the Stevenage BioScience Catalyst (SBC), accessing drug development expertise and facilities in an environment of active collaboration across industry and academia. Two of the first three UCLP projects to be transferred to the SBC are III programme led.

The global commercial cell therapy industry was estimated to have an annual turnover of $5bn by 2014, and we are well positioned to make a substantial contribution to this new market. We will work with TSB Catapult and commercial partners to implement new cell, gene and regenerative medicine therapies.

The development of amyloidosis therapy based on small molecule and humanised antibody combination has been chosen by GSK as its flagship project for potential adaptive licensing by the FDA and EMA, and is the subject of discussions aimed at reducing the time between demonstration of clinical efficacy and availability of the commercial medicine for patients.

2.4 Description of how the work Programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

Health Education: The III Programme includes a spectrum of education and training opportunities for junior and senior staff. Trainees in biomedical science have protected time and financial support to complete an MSc degree during their training. A newly designed BSc/MSc course in Applied Medical Sciences combines training in the biological sciences with particular reference to human health, so that graduates are familiar with clinical medicine. Similarly, a 4-year bench-to-bedside PhD programme combines research training with an education in relevant clinical medicine. Finally, III academics will provide a multidisciplinary training for clinical fellows and educate future clinical academic leaders.

Research integration: Working closely with population health infrastructure such as the UCLP CLAHRC we will utilise our strengths in diagnostics, new drugs and vaccines (supported by the IIT and BRI) informatics (Farr Institute @ UCLP) and clinical trials (IIT and UCL Institute of Clinical Trials incorporating the MRC CTU) to deliver the objectives of the AHSC. To process and assemble virus genomes from next generation sequencing data without the need for embedding complex computer technology in the NHS we will take advantage of ‘cloud based’ computation, and make maximal use of the new e-health environment being created within UCLP. This approach will lead to i) more effective treatment of HIV and HCV
infections, (ii) more targeted hospital infection control (norovirus infections), and (iii) better dynamic assessment and targeted management of community based viral outbreaks, notably measles and influenza.

**Public and patient engagement:** The Centre of Immunodeficiency is a joint initiative between Great Ormond Street Children Hospital and Royal Free London NHS Trust to provide clinical and research support for UK's largest cohort of patients with immune defects. We are an international Jeffrey Modell Centre and receive funds to raise the public awareness of immunodeficiency.

The IIT and BRI will host annual open lectures and education events to engage the public with the research and clinical activities, and consultations with patient groups will inform the development of these Institutes. Dedicated PPI support across UCL BRCs links patient panels to the UCLH BRC III Programme Board. The QMUL Centre for Public Engagement activities are extensive, involving i) local schools and young people, to inspire the next generation of learners ii) government, civil servants and politicians to inform policy development iii) cultural organisations, businesses and charities on community-based projects. Goals of this Centre include: setting new regional, national and international standards for the way universities engage with the public, and evaluation and measurement of the impact of public engagement work.

### 2.5 Description of how the theme/work Programme will involve and enhance multi-disciplinary and multi-professional working.

The III Programme benefits from strong links with corresponding BRC Programmes at UCLH, GOSH and Moorfields. These links will be further enhanced by alliance to NIHR Translational Research Partnerships (Joint and Respiratory), and NIHR initiatives in infection and rare disease research. Strategic links have been established with PHE, Wellcome Sanger Trust Institute (WTSI) and the Francis Crick Institute via the new IIT and BRI. One of our key objectives for the next four years is the co-location of investigators from UCL and LSHTM in a new BRI building. This building will incorporate a new model “open laboratory” to maximise the opportunity for integration into our intellectual and clinical environment.

Multidisciplinary working and knowledge sharing between academics, clinicians, nurses, patients and regulatory experts is essential for complex biological trials. The biological therapy projects of the III Programme are closely linked to the BRC Programmes of UCLH, GOSH and Moorfield Eye Hospital and will benefit from the IIT development providing additional state of the art facilities to produce cell clinical grade products. We have set up a UCLP cell and gene therapy consortium to bring together and link academic, clinical, and industry expertise to deliver novel translation to clinic. We have set up a strategic platform to bring together academic, clinical, and industry expertise to deliver novel translation to clinic. We will benefit from the IIT development providing additional state of the art facilities to produce cell clinical grade products. We have set up a UCLP cell and gene therapy consortium to bring together and link academic, clinical, and industry expertise to deliver novel translation to clinic. We will benefit from the IIT development providing additional state of the art facilities to produce cell clinical grade products.

We have built interdisciplinarity into training through CoMPLEX, UCL's centre for interdisciplinary research in the medical and life sciences, which brings together life and medical scientists with mathematicians, physical scientists, computer scientists and engineers to tackle the challenges arising from complexity in biology and medicine. Co-supervisory teams also link UCL with the Francis Crick Institute in a multi-professional capacity building initiative.

Health informatics cuts across the III work Programme and will be supported by the Farr Institute @ UCLP, and via existing facilities such as the LSHTM Centre for the Mathematical Modelling of Infectious Diseases and the Bloomsbury Centre (UCL and LSHTM) for genetic Epidemiology and Statistics. Bringing together epidemiologists, economists and mathematicians to address “big data” research questions will enhance our engagement with resources such as the national BioResource, as well Genomics England. We aim through this approach to enable patient stratification and develop novel diagnostic techniques.

### 2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the Programme.

The III programme will be led by an expert Steering Group of representatives drawn from across UCLP. The Steering Group will be responsible for the delivery of the Programme strategy as outlined in Sections 2.2-2.5, and in accordance with the AHSC’s strategic aims and objectives. The programme Steering Group Chair Professor Hans Stauss will be responsible for galvanising the community and reporting progress (including metrics) to the AHSC Planning and Performance Executive (as outlined in section 4). The Chair has an exceptional track record of delivery and a breadth of experience across research, education and clinical care, and will be supported by dedicated coordination expertise.

**Key organisational contributors responsible for delivering the III work programme:** UCLP, IIT, BRI, GOSH/ICH BRC, UCLH/UCL BRC, LSHTM, QMUL, Wellcome trust Sanger Institute, UCL School of Pharmacy, London Centre for Nanotechnology, the Francis Crick Institute

**Key individuals:** *Immune interventions to treat disease:* Mala Maini, Graham Foster, Paul Griffith, Emma Morris, Karl Pegg; Tom Powles, Sergio Quesada, Hans Stauss, Martin Pule, Lucy Walker, Brigitta Stockinger, Martin Birchall, Alex Safelian, John Gribben, Paul Falkland, Thorsten Hageman

**Prevention and control of infection:** Rachel McKendry, Rosanna Peeling, Andrew Hayward, Paul Kellam, Ibrahim Abubakar, Brendan Wren, Taane Clark, Nigel Klein, Francis Dobriniewski, Greg Towers, Judy Breuer, Deenan Pillay, Ali Zumla

**New therapies for inflammatory conditions:** Tom MacDonald, Tony Segal, Chris Denton, Mike Ehrenstein, Costantino Pitzalis, Mark Pepsy, Phil Hawkins, Massimo Pinzani, Lucy Wedderburn, Rachel Chambers, Claudia Mauri, John Ioannou

**Next generation diagnostics and personalised medicine:** Bodo Grimbacher, Siobhan Burns, Harry Hemingway, Stephane Hue, Kholoud Porter, Mark Lipman, Mahdad Nousaredeghi, Rosanna Peeling
UCL PARTNERS CANCER PROGRAMME

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership:
UCL Partners Academic Health Science Centre

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work Programme.
Cancer

2.2 Aims and objective of the theme/work Programme.

Programme aim:
The aim of the Programme is to harness world-class partnerships to integrate a more precision-based approach to cancer care in all aspects of the pathway, from targeting high-risk populations for earlier diagnosis through to stratifying patients for selected treatments, to patient-empowered, risk-adapted follow up. The Programme will bring together expertise in basic research, translational medicine, clinical trials, epidemiology and behaviour research to improve treatment and care, based on a personalised medicine approach. We are in a unique position to develop an integrated approach given the strength of established infrastructures, including: the NIHR/Wellcome UCLH Clinical Research Facility; the Cancer Research UK (CRUK) Cancer Trials Centre and Experimental Cancer Medicine Centres at Barts and UCL; the CRUK Centres at UCL and QMUL; and, the KCL/UCL Comprehensive Cancer Imaging Centre. Working through our integrated cancer system, London Cancer, our researchers have access to a population of up to 6.3 million. This has enabled us to exploit the harmonised NHS permission process across the system to attract industry partnerships. The outputs of our research harmonisation, together with our plans to bring state-of-the-art molecular genotyping into routine clinical diagnostics, will accelerate access to novel agents targeted at patients with specific genetic alterations.

1. Developing novel immunotherapy and gene therapy treatments:
Exploit our expertise in tumour immunology, immune-regulation, cancer vaccines, adoptive immunotherapy, T-cell engineering and vector design to develop new therapeutics. Research into cell death, inflammation and immunity is crucial for understanding tumourigenesis and development of resistance to therapy. We aim to develop biotherapeutics that target the TRAIL or CD95 death-receptor systems, specific ubiquitin ligase and de-ubiquitinase inhibitors, and immune-regulation as cancer treatments. We have already demonstrated the success of new immunotherapies, for example, the chimeric antigen receptor 19 Childhope Study. Novel approaches to target the immune cell components of the tumour microenvironment are being explored in both solid and haematological malignancies.

2. Prediction and stratification:
Continue to develop biomarkers to stratify patients for precision cancer treatment. This will be achieved using circulating tumour cell and circulating DNA for detecting minimal residual disease and monitoring clinical outcome. Genomic and epigenetic approaches will be employed to determine the importance of tumour heterogeneity in informing stratified care, determining mechanisms of resistance and predicting outcome. Research will focus on: defining the phenotype and genotype of ‘relapse initiating cells’ and the role of stem cells and genetic heterogeneity in drug resistance; and, developing ultra-deep, whole cancer genome sequencing approaches to rapidly characterise tumour heterogeneity and cancer clonal evolution during therapy.

3. Behaviour change:
In collaboration with the Faculty of Population Health, we will develop our interest in Cancer Behavioural Science, to tackle cancer deaths that can potentially be avoided by changing behaviour patterns. Research areas include understanding bio-behavioural mechanisms linking energy balance to cancer, and the role of obesity and weight loss on pre-cancers and post-diagnosis. Joint work between UCL and QMUL is exploring exercise as a primary treatment for prostate cancer. The CRUK Health Behaviour Research Group, which hosts three community implementation Programme grants, are already exploiting the rich research opportunities in screening and survivorship provided by London Cancer.

4. Early diagnosis, screening and survival:
Improving uptake of cancer screening opportunities and promoting earlier diagnosis through better understanding of factors that lead to cancer presenting as an emergency and radical redesign of diagnostic referral pathways in partnership with primary care is a priority for the London Cancer integrated system. The Department of Health (DoH) Policy Research Unit on Cancer Awareness, Screening and Early
5. Developing and improving technology to understand and treat cancer:
The Programme will link with the physical sciences to make advances in the detection, diagnosis and treatment of cancer. The KCL/UCL Comprehensive Cancer Imaging Centre, in combination with clinicopathological assessment, genomics and in-house optical proteomics techniques, will allow us to elucidate the molecular and physiological processes of cancer. Work by UCL has shown that inserting MRI into the diagnostic and therapy pathway of prostate cancer has considerable benefits, increasing detection rates of clinically significant disease in excess of 60%, with the practice standard identifying only one third. The benefits have been recognised by the National Institute for Health and Care Excellence (NICE) in the latest version of the Prostate Cancer Guidelines (in a consultation). We further plan to develop targeted multifunctional nanoparticles for tracking by two or more imaging modalities, allowing delivery of small molecule therapeutics to primary tumours and metastases, and to integrate imaging modalities with genomics and protein interaction analysis to understand cancer genome heterogeneity and predict individualised clinical outcome.

6. Phenotypic characterisation:
We are already setting standards for specialist pathology by tumour type for diagnosis across London Cancer, which will ensure that every patient’s tissue is subject to the same high standard of classification, including molecular genotyping and imaging, linked to clinical information. We aim to introduce gene panels through next-generation sequencing to give additional information at the same cost to the NHS so that more patients can be signposted to clinical trials at the earliest opportunity. In this way, we will not only increase the number of patients accessing the latest medicines but will also build the evidence base about efficacy and value at a population level, for changes in clinical practice using informatics.

2.3 Description of how the proposed Programme will contribute to AHSC aims.

**Partnership working:** In partnership with the Sarah Cannon Research Institute (SCRI), we are developing our early-phase clinical trial portfolios and associated translational research projects. Since 2010 the number of patients treated in early phase studies has increased from 35 to 120 per annum, and the number of open studies from 10 to 36. Our trajectory is to recruit 200 phase I patients/annum by 2016, increasing to 300/annum by 2019, creating one of the largest early phase cancer drug development Programmes in Europe. Our cancer molecular pathology service, UCL-Advanced Diagnostics, with the SCRI, has added a next generation diagnostic service to its existing service of high-throughput immunohistochemistry and the Fluorescence In Situ Hybridization test. The provision of these molecular tests from one site, alongside conventional microscopic findings, will allow an integrated reporting of pathology tests. This laboratory will continue to expand its next generation sequencing menu, and will introduce whole exome sequencing amongst other technologies.

**Industry engagement:** The Programme will continue to develop partnerships with industry to take forward promising discoveries from the laboratory into the clinic, spanning a range of therapeutic targets. Examples of successful industry collaborations include:

- Basic research in the area of drug-DNA interactions led to a spin-out company being developed, Spirogen Ltd, and the development of pyrrolobenzodiazepine (PBD) dimer drug SG2000 (SJG-136) through pre-clinical into early phase clinical trials in the UK and USA. The clinical trials have been enhanced by novel pharmacodynamics endpoints of DNA cross-linking and damage response developed in-house and run to GCLP at UCL. The first antibody-PBD conjugate will enter clinical studies in 2013
- A major limitation to Chimeric Antigen Receptor (CAR) T-cell therapy is the need to generate a bespoke therapeutic product for each patient. To develop universal T-cell therapy, we were awarded a €6m EU framework 7, starting Dec 2013. Celllects Therapeutics, a biotech SME with unique genome engineering technology, is a key partner in this goal. The pre-clinical part of the Programme includes development work to target adult and paediatric glioma, sarcoma, acute myeloid leukaemia and multiple myeloma funded from a variety of sources, including an innovation award from Johnson & Johnson.

**Informatics:** The Programme leads key work packages in over €60m of grants integrating clinical, omics and imaging data with workflows in cancer, and developing a European platform for hospital records use in clinical research (EHR4CR). The cancer Programme will work with the Farr Institute @ UCLP and the Bill Lyons Informatics Centre to bring together health records, phenotypes and genome sequencing data, in order to develop a rich source of outcomes-based research. Tumours from large cohorts of cancer patients will be well characterised for molecular phenotype, clinical risk factors and treatment received. This will facilitate increased patient participation, appropriately stratified, in relevant clinical trials and underpin...
2.4 Description of how the proposed Programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

The Programme will work with London Cancer to develop the integrated cancer system so that it functions as a ‘virtual comprehensive cancer centre’, bringing the same high quality of cancer diagnostics, treatment, supportive care and access to research and innovation to all patients. This approach will bring academics and clinician scientists, along with GPs, secondary and tertiary care providers, together to ensure that patients will be diagnosed using the best tests available and have access to the best care and treatment the system can offer. The Programme will explore opportunities to improve the clinical pathway and services, such as the development of specialist hubs for particular tumour tumours. This has already proved successful in the treatment of urological tumours.

Capacity building and leadership:

The award of the Proton Beam Therapy Centre has provided an opportunity to build an academic radiotherapy department that will focus on technological research and development, working with the physics and Engineering Departments at UCL and extending the implementation of novel radiotherapy techniques to treatment centres within London Cancer. The Centre will increase significantly our research and clinical care capabilities for difficult tumours (e.g. head and neck, and spine) and those where it is particularly important to reduce dose to other organs (e.g. in children). We will collaborate with the Manchester Proton Beam Therapy Centre and with our academic engineering and medical physics departments to embed continuous research and development in this cutting-edge facility.

The Programme will provide leadership in tumour types where we are nationally leading, including adult ALL trials, teenage and young adult cancer trials and lung and childhood cancers. For example, the London Sarcoma Service, sited across UCLH, Royal National Orthopaedic Hospital and GOSH, represents the largest sarcoma service in the UK. It is a nationally commissioned unit for primary bone tumours treating around 50% of patients with this disease in the UK annually. It is the largest single group worldwide contributing to international clinical studies in bone sarcoma.

Development of the workforce through education / training Programmes:

We will develop our education and training Programmes. The NIHR BRC Cancer Theme Clinical Fellowships will be incorporated into the CRUK Centre Clinician Training Programmes at Barts and at UCL. UCL’s NIHR BRCs have jointly agreed to contribute several clinical training fellowships per annum to establish a Clinical Fellowships PhD Programme at the Francis Crick Institute. New masters Programmes at UCL (Cancer Genomics, Cancer Nursing Research, Cellular and Gene Therapy), complementing the MSc Cancer course, and at QMUL (Cancer Therapeutics, and Molecular Pathology and Genomics), support career development for a range of professions. We will develop a ‘mini-MD’ Programme with laboratory and clinical exposure for all our post-graduate and clinical PhD and trainee fellows.

Public Engagement and Public-Patient Involvement:

This will be achieved through working with patient and other external groups and the appointment of leads...
for public engagement in cancer, working with CRUK. In childhood cancer, we are already working in partnership with parents and patients to both disseminate research findings, use advocacy with regulators and research funders to increase access to new drugs in Europe and to set future priorities, both nationally and at a European level. We will seek to emulate the success of the Eyes and Vision Programme in working with the James Lind Alliance to take the same leadership role for Cancer nationally, informing on priorities for patient treatment and care.

2.5 Description of how the Programme will involve and enhance multi-disciplinary and multi-professional working.

The UCLH/UCL BRC has cancer as one of four main themes and provides significant support for translational cancer research. Support has included recruitment of senior faculty to molecular pathology, and proposed appointments in neuro-oncology and lung cancer. GOSH/ICH has the only BRC solely focused on children. GOSH and UCLH treat more children and teenagers with cancer than any other centre in the UK, and joint work across the partners focuses on leading and coordinating clinical studies across age groups, conducting comparative studies on outcome, establishing a research unit for long term sequelae of interventions and using our biobanking capabilities to support the Genomics England 100k project in the plan to conduct whole genome sequencing on all child and teenage cancer patients.

The CRUK Cancer Trials Centre (CTC) and the Experimental Cancer Medicine Centre (ECMC) support translational research at UCL, and the Barts Clinical Trial Unit and ECMC provide analogous facilities and infrastructure at QMUL. The CTC works with clinical academic staff to design, conduct and analyse clinical trials. The new UCL Institute for Clinical Trials and Methodology, incorporating the MRC Clinical Trials Unit, will provide enhanced methodological capacity to support clinical studies. Future objectives include the development of small-scale early phase studies weighted towards translational endpoints; trials with Advanced Therapeutic Medical Products; and working with the UCL Cancer Institute to initiate whole exome sequencing in tumour samples from patients entering phase I-III studies, providing an opportunity to link genomics analysis to trial data, and to stratify patients to specific studies.

The Programme will work closely with the III Programme in immunology and gene therapy, studying the development of immune enhancing interventions for cancer and chronic infection.

Involvement with other Faculties:

Interdisciplinary research involving engineering and chemistry will exploit synergies of multimodality and multi-parametric imaging methods to improve tumour characterisation, treatment prediction and response assessment. We will link the physical sciences with clinical Programmes of image-guided treatment for prostate and brain cancer, exploiting the radiological phenotype to deliver new first-into-man treatments.

The development of robotic surgery techniques will improve the accuracy and efficiency of surgical treatment of solid tumours. A Programme of small molecule drug discovery will be developed with UCL Chemistry, the School of Pharmacy and the SCRI. The Programme will link clinical research with world-leading expertise in epidemiology at LSHTM, QMUL and UCL to support the development of longitudinal databases, allowing the success of changes to practice to be accurately assessed.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the Programme.

The Programme will be led by an expert Steering Group of representatives from across the partnership, responsible for the delivery of the Programme strategy, in accordance with the AHSC’s core strategic aims. The membership will be selected to ensure representation across the partners. The Chair (Professor Tariq Enver) will be responsible for galvanising the community and reporting progress to the AHSC Planning and Performance Executive (as outlined in section 4). Experts from clinical trials and experimental therapeutics (Jonathan Ledermann, Alan Hackshaw and Tim Meyer) and the key Programme areas will be involved in delivering the Programme:

**Key organisational contributors responsible for delivering the Cancer Programme**: UCLP NIHR/Wellcome UCLH Clinical Research Facility; CRUK Cancer Trials Centre and Experimental Cancer Medicine Centres at Barts and UCL; the CRUK Centres at UCL and QMUL; and, the KCL/UCL Comprehensive Cancer Imaging Centre, the GOSH/ICH translational cancer research consortium

**Immunotherapy/gene therapy**: Hans Stauss, Karl Peggs, Martin Pule, Claire Bennett, Adrian Thrasher, John Gribben, Thorsten Hagemann, Fran Balkwill, Nick Lemoine, David Taussig, Jeff Davies

**Prediction/stratification**: Charles Swanton, Tariq Enver, Stephan Beck, Adrienne Flannagan, Jude Fitzgibbon

**Behaviour change**: Jane Wardle, Robert West, Liam Burke,

**Early diagnosis and survival**: Jane Wardle, Stephen Duffy, Jack Cuzick, Peter Sasieni, Michel Coleman

**Technology to understand and treat cancer**: Tony Ng, David Hawkes, Mark Lythgoe, Shonit Punwani, Mark Emberton, Roland Illing
UCL PARTNERS CARDIOVASCULAR PROGRAMME

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership:
UCL Partners Academic Health Science Centre.

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work programme.
Cardiovascular

2.2 Aims and objective of the programme.

Programme aims: To achieve maximum global, national and regional impact for the benefit of patients with or at risk of heart disease or stroke our Cardiovascular (CV) programme will take the integrated CV system already operating across our NHS and University partnership to a new level of excellence, tackling fundamental questions. We will achieve this by further integrating: the research strengths of two CV institutes (at UCL and QMUL); the clinical expertise of three specialist cardiac hospitals (UCLH Heart, Barts and London Chest); and the translational infrastructure of the three BRCs at UCLH, Moorfields and GOSH and the Barts CV BRU; realising the transformative research and healthcare potential of hosting the National Institute of Cardiovascular Outcomes Research (NICOR -multiple national CV disease and device registries), and the Farr Institute @ UCLP.

Objectives: In the next 5 years, UCLP will capitalise on its world class research infrastructure to produce a step change in the translation of leading edge genomics, metabolomics, cardiovascular phenotyping, bioengineering and bio/patient informatics to enhance our understanding of disease pathophysiology and develop/evaluate the impact of novel diagnostics and therapeutic interventions. We will also promote this enabling platform to foster stronger industry partnerships. Our focus is on five cross-cutting themes, prioritising key unresolved questions, taking advantage of our unique concentration of patient populations with rare cardiovascular diseases and real world population cohorts.

1. CV Genomic Medicine into new diagnostics: UCLP attracts 20% of national commissioning for rare and inherited disease of the heart and circulation (e.g. familial hypercholesterolaemia, familial cardiomyopathies, lysosomal storage and mitochondrial disorders) and both hosts and links to extensive cohorts for commoner cardiometabolic conditions. This will allow us to link improved genotyping and enhanced phenotyping of these diseases to provide new insights into their pathogenesis and new therapeutic targets. We are positioned to take these studies to a new level by implementing generic consent and establishing a UCLP CV biorepository that draws on the latest approaches to the identification of CV biomarkers, e.g. metabolomics, contributing in the process to the NIHR Bioresource and rare diseases TRC. This approach will define new mechanisms for rare CV diseases that will inform the development of diagnostics and new therapies for stratified medicine for CV disease or its prevention over the next 5 years.

2. CV Target validation and therapeutic innovation: UCLP will integrate multiple-omics datasets and combine approaches such as Mendelian Randomisation with deeper phenotyping, leading-edge molecular physiology and pharmacology, and state-of-the art imaging to develop, validate and translate optimal therapeutic strategies for cardio-metabolic disease. This will draw upon our strong international and national partnerships (e.g. with the European Bioinformatics Institute) and will focus upon target validation in hypertension, ischaemia-reperfusion injury, obesity and disorders of heart rhythm. In the next 5 years, we will take forward into clinical trials a number of already identified novel or repurposed candidate molecules from our translational programmes, using this as a basis for new industrial partnerships (see below).

3. Novel device-based therapies for monitoring and treatment of CV disease: There has been a major expansion of device based diagnostics and treatments for CV diseases in the past 10 years. In partnership with Yale, we have recognised the potential to greatly expand academic/industrial partnerships in early phase CV diagnostic and therapeutic device development. This draws on the combined strengths at UCL/QMUL in biomedical engineering, the London Centre for Nanotechnology, imaging and informatics, as well as the new high throughput CV Centre at Barts Health. In the next 5 years, working with the team at Yale, we will replicate their highly successful CV Device Innovation Centre that will evolve as National centre for CV device development and clinical translation, establishing UCLP as the European preferred site for industrial partnership in CV devices research and implementation.

4. Translation of innovative CV prevention strategies into healthcare: The rich data of the NHS is underutilised. In the next 5 years, UCLP is uniquely placed to harness the enormous potential of the NICOR, housed at UCL, to link multiple national CV disease and device registries with primary care data,
hospital episodes and outcomes through our MRC e-Health Informatics Research Centre, the Farr Institute @ UCLP. This will create a unique, internationally leading health outcomes resource, spanning the entire life-course. We will use this to: (i) better understand, at scale, the risk factors that contribute to premature CV disease and the optimal timing for intervention; (ii) implement a new model of low cost ‘Real World’ clinical trials in CV prevention, that will have major appeal at a time when such innovation and increased affordability in trial design are vital to academia, industry partners and the NHS.

5. UCLP Translational Cardiovascular Academy: The CV Programme is committed to developing a skilled CV multidisciplinary healthcare team across the entire partnership and currently offers an excellent suite of short courses and modular Masters degrees. We will build on that provision through the recently launched MRes programme with a focus on translation for all clinical CV trainees and the integration of the best of our two BHF PhD programmes (UCL and QMUL). We will appoint an international CV clinician scientist to the Francis Crick Institute to act as a magnet for postdoctoral clinical trainees in that environment. We will develop the CV Academy further through the EU Marie Curie Cofund scheme and by attracting researchers from computing and biophysical sciences to our CV Device Centre. The CV Programme will actively support NHS Education England and Genomics England in the proposed capacity building programme to transform the capability of the NHS to adopt Genomic Medicine.

2.3 Description of how the proposed programme will contribute to the aims of the AHSC.

Research Excellence: The UCLP CV programme has a strong academic foundation and is a major contributor to the international standing of UCLP with over 7000 CV publications (2006-12 Web of Knowledge), many in the highest impact journals, and research awards in excess of £176m over the past six years. These metrics are comparable to the leading US CV research centres. We recognise that our challenge is to harness this potential to match the enterprise culture of the leading US centres in translating academic excellence into stronger innovation, commercialisation and industrial partnership. This will be achieved by extracting more from strategic integration of our infrastructure, extending our reach and partnerships and by a palpable change in the culture of partnership with industry.

Integrating the enabling infrastructure for the CV Programme contribution to UCLP: To deliver the UCLP CV programme we will harness and better integrate the potential of our extensive collaborative NIHR infrastructure, UCLH BRC/BRUs, the Barts BRU, the NIHR Bioresource and our clinical research facilities, to accelerate translation. In addition, we will ensure that the full potential to transform CV healthcare that derives from hosting the NICOR, and the Farr Institute @ UCLP is realised. We will add further value from our national and international partnerships e.g. NIHR partnerships, Yale, Genomics England, Quintiles and multiple industrial partnerships (see below).

Global Reach: At UCLP a key international partnership is the joint Yale/UCL collaborative. A particular focus is CV device-based innovation which is providing a pipeline of devices ready to go into human trials but the collaboration also extends to genomics and medicinal innovation. In Genomic Medicine we lead major multi-university partnerships, with over 24 nations worldwide investigating the genetic architecture of blood pressure, coronary disease and arrhythmias. The UCL Hatzer CV Institute’s partnership with the University of Cape Town enables access to cohorts on the African continent facilitating research e.g. on ischaemic pre-conditioning in diabetes. With the Utrecht Medical Centre we are expanding our biobanks linked to imaging and health records to contribute further to the NIHR Bioresource.

Partnership working: UCLP’s BRC/BRU’s infrastructure is a major contributor to multiple national partnerships across CV medicine thereby helping to harness the full potential of NIHR infrastructure. Our partnerships include: stratified medicine (Cambridge), CV Genomics, pharmacogenetics (Barts, UCLH, Leicester, Oxford, Imperial), rare disease (NIHR Translational Research Collaborative), familial hypercholesterolaemia (GOSH, Barts), cardiovascular imaging (GOSH, Barts, UCLH, Brompton, Leicester and Oxford), abdominal aortic aneurysm (Leicester), medical devices and technology (Barts/GOSH, UCLH), hypoxia (Southampton), angiogenesis and retinal vasculature (Moorfields, see UCLP Eyes and Vision), ischaemia reperfusion/conditioning (all UK CV BRC/U’s) and the MRC/NIHR National Phenome Centre (UCLH, Barts, Imperial and Kings). Such networked capability adds significantly to the AHSC’s aims.

Industry engagement and commercialisation:
Building on work already undertaken within the BRC/BRUs, we will continue to develop the culture of entrepreneurship and enterprise within the CV Programme with a focus on improving our routes to commercialisation of intellectual property and technology transfer, as well as promoting our capacity and capability to attract “reverse technology transfer”, i.e. inflow of external IP for development within UCLP through joint ventures and shared licensing. We will at least double the number of Pharma/SME partnerships, patents and licensing deals over the next 5 years. Specific targets to develop further are: Genomics England: We have multiple industrial partnerships in the field of stratified healthcare. Genomics England, the Department of Health company leading whole genome sequencing of 100,000 patients is based within UCLP, and an early pilot of rare disease will be facilitated, in part by drawing on deeply phenotyped families from the CV Programme.

The pharmaceutical industry: The UCLH/UCL BRC funds translational projects at the Stevenage Biocatalyst which we will draw upon to increase target validation of new therapies building on existing partnerships.
These include with Novartis (CRP inhibition, ARB/NEP inhibition), GSK (our own molecules targeting amyloid), AMGEN/ Sanofi/Pfizer (all PCSK9 inhibitor studies), Johnson & Johnson (new anticoagulants) and Bristol Myers Squibb and MSD (gliptins). We will also develop our major partnership with Quintiles Transnational which offers UCLP access to all trials managed by them in the UK. These partnerships contribute to the cross-cutting multi-professional working of UCLP with our MRC Clinical Trials Unit and NIHR Wellcome Trust/Wolfson CRF to enable us to expand our experimental medicine capacity and explore new real world trials with industry.

Device manufacturers: UCLP has led major device innovation of percutaneous valves and partnered international small-medium enterprises to develop multiple approaches for device monitoring and therapy of hypertension and cardio-metabolic disease. There are more than ten on-going industrial device trials including novel percutaneous therapies. This is a very strong aspect of our CV Programme which we will double in size over the next 5 years via our partnership with Yale to develop the CV Device Innovation Centre. As evidence of our commitment to both development and implementation, with Ardian we led the UK limb of the first randomised controlled trial of renal denervation, established the Joint UK Societies Guidance on this approach and are now leading implementation in the NHS. At NICOR we have established the UK Registry on this procedure (and three others) demonstrating how the comprehensive capabilities of the CV Programme can help drive and assure effective service innovation. Working closely with the National Office of Clinical Research Infrastructure we will help to showcase the UK as an excellent place for device-based research and therapeutic development.

Imaging companies: UCLP has the largest CV imaging practice in the UK and the highest impact research output with extensive research and development partnerships around magnetic resonance imaging and CT with Siemens, Philips and Circle. Fundamental physics and engineering will be used to extend the capability of MRI in the non-invasive phenotyping of CV disease. This is integral to deeper phenotyping and device-based therapy and underpins multiple aspects of the CV Programme.

2.4 How the proposed programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

Integrating clinical care with research and training:
The UCLP strategy for our new Integrated CV System aims to bring together NHS tertiary clinical services and related clinical academic expertise from UCLP at the new 60,000 m² St Bartholomew’s Hospital (£400m) with the ambition to make this the premier centre for CV therapeutic innovation over the next five years. To facilitate this UCLP has integrated CV activity across our NIHR infrastructure and fostered strong collaborative links specific to experimental medicine and clinical trials across both UCLH, QMUL, Barts (CV inflammation, CV Pharmacology, electrophysiology, cardiovascular imaging) and Moorfields (angiogenesis). In preparation we have opened new research infrastructure with a new £25m Heart Centre at QMUL and a new adult CV phenotyping centre for physiology studies adjacent to NICOR and Olympic Legacy Institute of Sport, Exercise and Health at UCL/UCLH. Our plans, once approved, will create one of the largest tertiary CV Centres in Europe providing the opportunity for the highest calibre integrated NHS service, research and training aimed at excellence in patient care and rivalling the major US centres in quality and scale. Whilst are plans are not contingent upon this development, they will be greatly enhanced by it.

UCLP Informatics Platform linking primary care data with outcomes:
Increased bioinformatics capacity and capability will be fundamental to realising the potential of major NIHR investment into the MRC-NIHR National Bioresource Phenome Centre and genotyping. UCLP’s translational CV programme is a key theme within the Farr Institute @ UCLP and offers a multiprofessional training academy for bioinformatics and computer science capacity. The UCLP e-Health agenda will deliver improved records and data linkage which will identify better care pathways capitalising upon our extensive CV Registries held at NICOR and reaching out across primary care to enhance patient care. In addition UCLP hosts a unique and extensive set of epidemiological cohorts offering important insights into life course health (e.g. Whitehall II, MRC 1946 Birth Cohort). An ambition for this partnership is to integrate electronic health records to further enrich these datasets for affordable longitudinal follow-up and undertake real world CV trials where patients are followed remotely through e-Health Primary Care linkage as a way to enhance evidenced-based care linking with clinical Practice Records Datalink to facilitate this.

Multi-professional Education and Training.
To maximise the educational potential from the UCLP AHSC we will integrate undergraduate medical student and postgraduate clinical scientific training from UCL and QMUL at the Barts site. We will develop new programmes that reach across the multidisciplinary team in the AHSC to provide the highest calibre CV team across the partnership. We are integrating our BHF Non-clinical PhD programmes and have just begun offering a Masters of Research to all UCLP clinical trainees. This is alongside established short courses and other degrees extending across the multi-professional healthcare team and international programmes such as Cardiology, Diabetes and ‘Nephrology at The Limits’, Yale/UCL Device Summit and the John Vane Memorial Conference our aim is to build capacity in Cardiovascular clinical science, especially in experimental medicine, aligned to our BRC/BRUs.

Public Engagement and Public-Patient Involvement:
2.5 Description of how the theme/work programme will involve and enhance multi-disciplinary and multi-professional working.

**UCLP Multidisciplinary working:** Across UCLP there are very strong linkages between the CV Programme and CV interests in the other Programmes, e.g. Eyes and Vision (retinal vasculature and angiogenesis), Neuroscience (stroke), Child Health (congenital heart disease) and III (periodontal disease and CV risk). Many facets of the CV programme benefit from strong inter-disciplinary linkage e.g. clinical trials and device-based therapy. Our proposed Device Centre will connect clinicians with physicists, bioengineers, imagers and trialists focused on cutting-edge innovation (UCLP hosted the UK symposium on renal denervation). We benefit from an extremely well established and proven infrastructure across UCL/UCLH/QMUL together with more recent additions through the Yale/UCL collaboration and Institute of Sport, Exercise & Health, the latter focussed on translating understanding of physiological adaptation in elite athletes into novel approaches to improve cardiovascular disease prevention and rehabilitation.

**UCLP multi-professional working:** UCLP will continue to develop and train healthcare teams, researchers and educators from diverse disciplines to ensure the extended team are ready to translate innovation into practice building off programmes of remote monitoring of patients in the community. This will enable UCLP to harness the capacity of the healthcare workforce to allow us to adopt innovative trial designs making studies across UCLP more affordable and closer to real world clinical CV care. The CV Programme will harness the multi-professional team to implement innovative stratified medicine initiatives and maximise life-course CV prevention.

**The Quintiles Prime Site Clinical Trials Partnership:** This multidisciplinary partnership originated from QMUL where we concentrated all possible trials placed in the UK by Quintiles in a high performance site management organisation. This is led from the CV Programme on behalf of UCLP and currently manages 33 trials across all therapeutic areas and has been extended this year across all UCLP Programmes. This Prime site consistently performs in the top 25% of such trials hubs worldwide and exemplifies the AHSC’s capability to attract new trial opportunities for our patients and extend a successful endeavour across the multi-professional team at UCLP.

2.6 Leadership, key individual and organisational contributors responsible for programme delivery.

The Cardiovascular Programme will be led by an expert Steering Group of representatives drawn from across the UCLP partnership. The Steering Group will be responsible for the delivery of the Programme strategy as outlined in Sections 2.2-2.5, and in accordance with the AHSC’s strategic aims and objectives. The membership will ensure appropriate, discovery, clinical, applied, evaluation, education and enterprise expertise, and will include a patient representative.

The CV Programme Steering Group Chair (Professor Mark Caulfield) will be responsible for galvanising the community and reporting progress (including agreed metrics) to the AHSC Planning and Performance Executive (as outlined in section 4). The Chair has an exceptional track record of delivery and a breadth of experience across research, education and clinical care, and will be supported by dedicated coordination expertise.

**Key Organisations:** UCL, QMUL, LSHTM, Institutes of Ophthalmology and Child Health, BRCs at UCLH, GOSH and Moorfields and Barts CV BRU, Quintiles, Genomics England.

**Key individuals** whose work will achieve the aims of the AHSC include:

**Translating Genomic Medicine into CV healthcare:** Mark Caulfield, Aroon Hingorani, Panos Deloukas, Perry Elliott, Steve Humphries, Pier Lambiasi, Bill Mckenna, Patricia Munroe, Philippa Talmud, Andrew Tinker, Shu Ye and Mike Barnes.

**CV Therapeutic Innovation:** Amrita Ahluwalia, Rachel Batterham, Derek Hausenloy, Derek Yellon, Chris Thiemermann, Adrian Hobbs, Christiana Ruhrberg, Ken Suzuki, Mark Caulfield, Aroon Hingorani, Bryan Williams.

**Device-based innovations for monitoring and therapy of CV disease:** Andrew Taylor, Anthony Mathur, James Moon, Bill McKenna, Mike Mullen, Steffen Petersen, Richard Schilling, David Wald, Bryan Williams.

**CV prevention strategies into healthcare:** John Deanfield, Harry Hemingway, Liam Smeeth, Aroon Hingorani, Mark Caulfield, Bryan Williams.

**Creating the UCLP Translational CV academy for research and education:** Jean McEwan, Peter Scambler, Philippa Talmud, Tim Warner.
UCL PARNTERS EYES AND VISION PROGRAMME

1. DETAILS OF THE PROPOSED ACADEMIC HEALTH SCIENCE CENTRE (AHSC)

Name of the English NHS Provider/University Partnership:
UCLPartners Academic Health Science Centre

2. THEME / WORK PROGRAMME

2.1 Name of the theme/work Programme.

Eyes and Vision

2.2 Aims and objective of the theme/work Programme.

Programme aim: The Eyes and Vision work Programme will deliver improvements in the visual health, quality of life and wealth of the nation, translating through to innovations in informatics, diagnostics, monitoring and therapies. Ultimately we continue our original aim which is to change lives for the better in London, the UK and the world.

Objectives: Within six established cross-cutting interdisciplin ary groupings dedicated to supporting ophthalmic translational medicine in common and rare diseases, we will harness the world-leading expertise and technologies within our NIHR Moorfields BRC along with the successful clinical and research partnerships that we have already made and are continuing to expand with within UCLP, Francis Crick Institute and other UK and international centres of excellence in the following areas: 1) Regenerative therapies and novel drugs, 2) Gene therapy, 3) Novel devices, including diagnostic and surgical, 4) Imaging and functional assessment of the eye, 5) Inflammation and Infection, and 6) genotyping/phenotyping and informatics

Key improvements we seek to achieve in specific disease areas are:

1. Retinal Disease – major cause of blindness in the developed world:

   Wet age-related macular degeneration (AMD): Through new diagnostic tools, improved early detection of disease and new therapies, we will reduce the burden of visual impairment in wet AMD patients who see worse than 6/12 (those who cannot read a sign within six feet) from 60% to less than 30%. Dry AMD: We will deliver improved tools to assess progression risk and at least one effective therapy for dry AMD such that over 10% of patients will have a significantly slowed rate of disease progression. Diabetic Retinopathy: We will improve response rates to therapy from the current rate (30%) to 50-60% through new agents to reduce the growth of new blood vessels, their leakage and consequent visual loss. Uveitis: Through new diagnostic and integrated therapeutic approaches we will improve the patient response rate from 65% to 85%. Inherited retinal disorders: Using our ocular gene therapy approaches, we will have a significant impact on childhood blindness due to inherited disorders. Peripheral vision training: By improving the effectiveness of peripheral vision training for patients and by identifying which individuals are able to self-train, we will reduce the impact of AMD on quality of life by 30%.

2. Glaucoma – the major cause of irreversible blindness in the world:

   Detection: Diagnostic innovations will reduce the percentage of individuals with undiagnosed glaucoma from 50% to 25%. Glaucoma surgery: By improving surgery and anti-scarring drug delivery we will increase the most stringent definition of success in glaucoma surgery from 20% to over 50%. New devices in development have the potential to reduce world blindness from glaucoma by more than 500,000 over a decade if fully implemented with the help of the UCLP.

3. Corneal and eyelid disease – Major cause of attendances to primary care:

   Gene therapy for the cornea: Using corneal gene therapy we will obviate the need for corneal transplants in 30% of patients with blinding endothelial disease. New techniques to treat ocular surface disorders: we will harness our expertise in imaging, immunology, anti-scarring treatments and corneal pathology to combat conjunctival cicatrization (i.e. Stevens-Johnson syndrome and pemphigoid). We will also reverse blinding corneal vascularisation, and use image-labelled autologous immune cell trafficking to donor cornea post-transplant to quantify graft rejection risk and stratify immunosuppression. Eye-lid reconstruction: With novel implanted synthetic materials, we will replicate eyelid movement in patients with congenital disease, neurological disorders or after trauma to restore the eyelid’s ability to protect the front of the eye.

4. Cardiovascular disease: By imaging the retinal circulation, we will provide an experimental medicine platform to help improve tissue perfusion at the level of the microcirculation. Our studies may also provide diagnostic tools for stratifying patients for CV trials, and response to anti-inflammatory agents.

5. Neurodegenerative disease: Changes in the eye can give insights into non-ocular disorders and help...
predict the outcome of therapy for Stroke and Alzheimer’s patients. With cell-level anatomical and functional imaging, we will work with colleagues at the UCL Institute of Neurology and the Francis Crick Institute to improve the precision of diagnosis and prognosis in a wide range of neurodegenerative disorders.

2.3 Description of how the proposed theme or work Programme will contribute to the aims of the AHSC.

Global reach (OpenEyes, Open world): Informatics is one of the keys to improving global visual health – both in the developed and developing world. Worldwide, 80% of visual impairment is avoidable. We can help provide the clinical detection tools, monitoring and training required to combat sight loss through sophisticated informatics systems. Our open-source electronic patient record system, OpenEyes, was recently presented to the Secretary of State for Health through UCLP as an example of a world-leading initiative. The system has been selected by Orbis (one of the world’s largest NGOs in Vision) in a highly competitive tender involving 18 systems from all over the world. This endorsement will bring other opportunities for collaboration in research, teaching and patient care. In addition, we are working with the Queen Elizabeth Diamond Jubilee Trust (http://www.jubileetribute.org/the-trust/), where Eyes and Vision have become the major investment focus of the UK Department for International Development (£50m), and through the Commonwealth (£40m) with the aim of having a major impact on avoidable blindness by 2020 through projects for trachoma, diabetic eye disease and childhood eye diseases. This may also link through to the Common Health for the Commonwealth launched by Lord Kakkar at the Commonwealth ministers’ meeting in Geneva. OpenEyes, UCLP informatics initiatives, UCLP research leaders (including the London School of Hygiene and Tropical Medicine) will be contributing to this major initiative, with UCLP as an anchor partner. Through the NIHR Moorfields BRC, Eyes and Vision has established and signed a major research and strategic alliance (one of only three) with the US National Institutes of Health and recently extended to Guangzhou University, China, to provide a framework for sharing the research strengths of each institution on immune-mediated diseases of the eye. This has aided career paths development, and design of jointly developed clinical research studies giving patients access to a novel treatment. The consortium will create a potential patient catchment area for inflammatory eye disease of over 40 million people. Our ambition, over the coming three years, is to establish further collaborations. OpenEyes will be used across our UK vision collaborating sites and the NIH, and will extend to all collaborating partners.

Partnership working: The UCLP Eyes and Vision Theme is the world’s Number 1 ranked research partnership in Ophthalmology. It is the only Number 1 ranked NHS/University research partnership in the United Kingdom (McKinsey 2003, Boston Consulting group 2013). It is also the partnership with the highest number of joint NHS/University highly ranked publications in the UK (RAND Europe). We have successfully partnered with Bristol Hospitals and Bristol University for our inflammation Programme, and we are now seeking new national and international partnerships to further strengthen our research and education bases. Our rapidly increasing industry partnerships are outlined below.

Industry engagement: Eyes and Vision has increased industry partnership funding by more than 400% over the last 5 years, one of the most successful in the UK. The ground-breaking partnership between the UCL Institute of Ophthalmology and GSK was renewed in January 2012 at £1m per annum for 3 years with the potential to extend for a further 2 years. GSK’s entire proprietary molecules compounds are being used to explore biological mechanisms for target validation in ophthalmic disease. The collaboration with GSK includes the funding of full-time research staff and has led so far to the nomination of several clinical-track candidates. Our London Project to Prevent Blindness, developed in collaboration with Pfizer, has helped to keep Pfizer located in and investing in the United Kingdom. Further large-scale industrial collaborations with major international companies including Roche are currently in discussion. Several of these companies have sought out our theme because of our pre-eminence in world research. Our Theme has launched a “Challenge Fund” to industry and other potential partners. Our new approaches will inform interactions with the SBC, located next to GSK. The SBC has a focus on novel therapeutics, biomarkers and cell technologies and will provide access to the development groups within GSK to allow the rapid development of clinical product and entry into early stage clinical trials.

Personalised medicine: Eyes and Vision is uniquely poised to develop personalised medicine. The extensive work on genotype (the Eyes and Vision theme has cloned more genes than any other grouping) and the ability to image at the cellular level and provide large-scale clinical information through OpenEyes for analysis will allow us to personalise care for the individual. Currently, through our BRC, we are the national coordinating centre for the NIHR Rare Diseases initiative for ophthalmic conditions. This information will also enable us to stratify clinical trials and potentially deliver early-phase trials that take a quarter of the time, halve the number of patients, recruit much faster and create twice the chance of a successful outcome for licensing. We are committed to providing the best care and treatment plan for individual patients.
2.4 Description of how the proposed theme or work Programme will contribute to the further integration of research, health education and/or patient care and how this will lead to improvements in patient care.

**Informatics:**
The informatics thread running through this application will bring together and integrate research, health education and patient care. The research on data obtained from many patients and brought together by the informatics base will guide best patient care. It will do this by informing both the professional and the patient (through the patient portal) about the different outcomes with different treatments from a huge database and thus allow decisions to be made about the best option personalised for the individual patient. If the genotype is available then that too can be integrated into the data and possibly assist in predicting the response to different treatments. Through the patient portal the patient will also have this information to inform choices. Education can also be linked into this system to assist the clinical professional (e.g. production of research-based guidelines) or the patient. Furthermore, OpenEyes will be used to link devices and patients with huge potential savings in time.

**Patient and Public Involvement:**
Through local, national and international platforms we harness the experiences, perceptions, needs and concerns of the patient to inform all that we do in education, research and patient care. Our researchers from fellowship level to consultant develop research Programmes and projects in collaboration with patients so that primary outcome measures are jointly informed by healthcare professionals and patients. We provided a leadership role in the national Priority Setting Partnership (PSP) for Sight Loss and Vision, overseen by the James Lind Alliance and coordinated by Fight for Sight, bringing together for the first time all patient-support charities in the sight loss domain, as well as the Royal College of Ophthalmologists, College of Optometrists and Vision 2020. In 2012, the PSP oversaw a national survey of healthcare professionals, patients and their families asking about unmet need in the prevention, diagnosis and treatment of sight loss. In October 2013, on the eve of World Sight Day, we will formally publish the outcomes of the survey – which has been the largest ever for the James Lind Alliance, producing 4,461 possible questions for research which have all been assessed and prioritised by patient and healthcare discussion groups. The results will inform the priorities for eye research in the UK for many years to come. Moreover, the experience of working together as a sector has had lasting impact about the wide benefits of ensuring that the patient voice is always sought. We are influencing the international arena through our work in patient and public involvement, particularly through the Association for Research in Vision and Ophthalmology, the leading international organisation for vision research with over 12,000 members.

**Research capacity development and talent management:**
UCLP provides opportunities for cross-disciplinary working which enhances the expertise available to combat eye disease. We have established joint research projects across UCL including Great Ormond Street Hospital and the Institute of Genetics and we have recruited, through a UCLP scheme, the first of several clinical research fellows who will work between Moorfields/UCL Institute of Ophthalmology and the Francis Crick Institute on an aspect of eye research. We are embarking on a Programme of expansion to meet growing need, particularly in informatics and imaging, and seek to recruit 15 new Faculty positions during the remainder of the decade.

We will build on our experiences of recruiting 12 NIHR Integrated Academic Training academic clinical lecturers (ACLs) and academic clinical fellows (ACFs) in vision research and of providing mentoring to them in the development of their careers. They provide the immediate pool for the research leaders of the future. We provide an annual training day for all national ophthalmic ACLs/ACFs with the aim of creating collaborative research platforms and support mechanisms for future leaders.

2.5 Description of how the theme/work Programme will involve and enhance multi-disciplinary and multi-professional working.

**Sensory neuroscience:** The commonalities between Hearing and Balance (‘ENT’) and Eyes and Vision provide significant opportunities for joint working, together with sensory neuroscience in the Institute of Neurology, the Institute of Cognitive Science and the Centre for Deafness Cognition and Language research at UCL. The UCL Faculty of Brain Science has established sensory systems as a strategic priority. We contribute to links between UCL and QMUL, in themes such as sensory optimisation in dementia and regeneration of the sense organs.

**Avoidable morbidity:** We are also developing a joint Programme of disease prevention to meet the challenge of avoidable morbidity, which will encompass multiple areas across Neuroscience, Mental Health, Hearing and Vision. Focusing on early diagnosis, shared risk factors and on behavioural change and health educational strategies, the Programme will link the Behaviour Change Unit at UCL, the Wolfson Institute of Preventive Medicine at QMUL, and the expertise in epidemiology and Public Health in UCL and QMUL.

**Open-Source informatics:** We will take advantage of the development in electronic patient records with research capability, to engage with industry around common disorders. Examples of this include OpenEyes, our open-source project producing a world-class ophthalmic electronic patient record system (http://www.openeyes.org.uk/), the basis of which can be used to develop multisystem informatics in...
association with the Farr Institute @ UCLP, the EHIRC and the new proposed UCLP open-source informatics Institute.

**Novel micro-devices:** One of our key Programmes is currently shortlisted for NIHR i4i funding. Our bold aim within this highly multidisciplinary Programme involving UCLP Institute of Biomedical Engineering, UCL School of Pharmacy and industry is to deliver a new microsurgical device for glaucoma which lowers the pressure to 10mmHg, remaining fully functional for 10 years and above of all can be surgically implanted within 10 minutes, which is now a real possibility due to multidisciplinary working.

2.6 Description of leadership and key individual and organisational contributors with responsibility for delivering the theme/work Programme.

The Eyes and Vision theme will be led by an expert Steering Group of representatives drawn from across the UCLP partnership. This will include the leadership team for our existing NIHR Moorfields BRC. The Steering Group will be responsible for the delivery of the Eyes and Vision strategy, and in accordance with the AHSC's strategic aims and objectives. The membership will incorporate appropriate discovery, clinical, applied, evaluation, education and enterprise expertise, and will include a patient representative.

The Programme Steering Group Chair (Professor Sir Peng Tee Khaw) will be responsible for integrating the community in the Eyes and Vision strategy and reporting progress (including agreed metrics) to the AHSC Planning and Performance Executive (as outlined in section 4). The Chair has an exceptional track record of delivery and a breadth of experience across research, education and clinical care, and will be supported by dedicated coordination expertise.

**Key individuals and organisational contributors responsible for leading the Eyes and Vision theme:**

**Organisations include:** UCLP, Moorfields and UCL Institute of Ophthalmology, GOSH and ICH, UCL School of Pharmacy, LSHTM, UCL Business

**Individuals:**

**Regenerative and gene therapies:** Peng Tee Khaw, Robin Ali, Pete Coffey, Julie Daniels, Lyndon Da Cruz, James Bainbridge, Steve Brocchini, Astrid Limb, David Shima, Marcus Fruttiger, David Charteris, Andrew Dick, Matthew Burton, Frank Larkin, Anthony Moore

**Novel devices (including surgical techniques):** John Marshall, Peng Tee Khaw, Fred Fitzke, George Saleh, Bruce Allan, Romesh Agunawala, Keith Barton

**Imaging and assessment of the eye:** David Garway-Heath, Chris Dainty, Gary Rubin, Marko Nardini, Philip J. Luthert, Steven Dakin, Michael Crossland, Aachal Kotecha, Jugnoo Rahi, Andrew Stockman, Adnan Tufail, Nicholas Strouthidis, Joe Carroll

**Inflammation and Immunotherapy:** Andrew Dick, Richard Lee, David Shima, Clare Bailey, James Bainbridge, John Dart, John Greenwood, Carlos Pavesio

**Genotyping/phenotyping and informatics:** Anthony Moore, Paul Foster, Shomi Bhattacharya, Frank Larkin, Bill Ayward, Vincent Plagnol, Tunde Peto, Philip J.Luthert
6. INCLUSIVITY AND DIVERSITY (2 pages)

Please provide evidence of the proposed AHSC’s commitment to equality and diversity including:

- How the partnership will realise the full potential of talent from across the whole workforce including promotion of equality and diversity;
- The partnership’s strategy for meaningful patient and public involvement (PPI) in the delivery of the objectives of the proposed AHSC;
- The partnership’s strategy for meaningful patient and public engagement (PPE).

Commitment to realising the full potential and talents of its workforce:
Our AHSC is committed to realising the full potential of its workforce and that of its constituent organisations. A key part of our strategy is the provision of comprehensive leadership development Programmes that embrace core institutional values that promote equality and diversity. An example of such a Programme is UCLP’s own multidisciplinary Staff College Leadership Programme, now in its third year, that draws on experience in other sectors, most notably the armed services. In addition, UCLP continues to complement such training with national initiatives such as the NHS Leadership Academy, both in London and nationally, to support current leaders within our network. The AHSC core leadership team members recognise the importance of role modelling the right leadership behaviours to complement our educational provision.

UCLP and partner institutions are deeply committed to promoting a diverse and inclusive workforce, the means chosen reflecting institutional staff profiles and the communities they serve. UCLP has a generous maternity and adoption leave policy and flexible working practices that help to retain a majority of women as Directors. Our NHS partners have an enhanced duty under the Equality Act 2010 to consider the diversity of their workforce. Our academic partners are committed to progressing their Athena SWAN status which seeks to advance the representation of women in science, engineering and technology. All three HEIs are Athena SWAN Bronze Award holders and are engaged in ambitious plans to achieve Silver status, recently achieved by six UCL Biomedical Divisions. Other initiatives to promote equality and diversity include: QMUL, in partnership with other London institutions, has established the ‘BM-Entor’ mentoring scheme where senior academics mentor Black and Ethnic Minorities (BME) academic staff; UCL’s Academic Careers Office jointly supported by the UCLH/UCL BRC seeks to promote, support and develop all aspects of academic and clinical academic careers. Key initiatives include the ‘Future Fifty’ scheme, which provides mentoring to early career researchers, and the Academic Role Models project, which recognised individuals nominated by their peers as having had a positive impact on others. Of the 40 role models identified, 53% were women. In recognition of its focus on improving the career development and management of researchers, UCL has received the European Commission HR Excellence in Research Award, along with six other UK universities. LSHTM’s Talent and Educational Development Unit and QMUL’s Learning Institute enforce a robust workforce development strategy.

These are just examples of how UCLP AHSC organisations are promoting the diversity and equality agenda. However, as a partnership, we recognise there is even further potential to impact the organisations in which we work and populations we serve through sharing best practice and our successes in workforce interventions. An example of such an approach is the nursing EXCEL Programme which involved partner organisations coming together to solve a leadership gap in developing ward sisters. After 6 months, the Programme was launched and the first cohort appointed to participate in a 4-year accelerated ward sister development Programme. A second cohort has since been recruited. The power of the partnership to address such issues is tremendous and we will continue to capitalise on this potential as an AHSC.

UCLP’s strategy is grounded in meaningful patient and public involvement (PPI). We see this as the key to understanding the needs and experiences of patients, pursuing a health service and research agenda that genuinely responds to patients, service users and carers and strengthens accountability to our local communities, fostering a sense of ownership. Our PPI strategy has three underpinning goals:

i) To strengthen user involvement (including decision-making, diffusion of best practice, consultation and information)

ii) To improve the patient experience (e.g. implementation of innovation, evaluation and communication)

iii) To gain patients perspective of clinical need to inform our research priorities and their relevance

UCLP has established formal PPI representation across our governance structure, including, for example, 3 patients on London Cancer Board. The AHSC Sub-Boards (Education, Research, Health Generation and Informatics) all have patient representatives. UCLP strives to have patients or members representative of our population on interview panels, and uses a “patient and population focus” as a key competency for assessment of applicants. A dedicated full-time manager, a patient herself, has recently been appointed to lead on patient experience. Further specific initiatives are detailed in the six Programmes.
Ahsc strategic PPI priorities (and indicative initiatives):

- **Share best practice**: A key UCLP role is to facilitate the diffusion of best practice by drawing on the experiences and best practice of our member organisations. An indicative example is a UCLP User Involvement ‘toolkit’, developed to provide a guide for all our partners on how to ensure patients, carers and the wider public are involved in the organisation at all levels and stages of development. UCLP has developed links to patient governors and Healthwatch organisations locally, and will build on this to develop a forum for effective PPI and engagement in early 2014.

- **Promote a ‘citizen science’ approach**: UCLP is a proponent of ‘citizen science’, where the role of PPI in research involves more than passive participants, but true collaborators – an approach which underpins our Lifelong Health cross-cutting theme. This encompasses the ‘quantitative self’ concept, where people use new technology to collect multiple forms of data during daily life, as well as ‘citizen science’, with the public directly involved in data collection or analysis. UCLP has also directly enabled and provided support for patient-led research, harnessing project design expertise whilst giving patients autonomy to carry out their own research. UCLP’s strategic partnerships with key charitable groups are providing useful insights here, e.g. ShiftMS, Macmillan and AgeUK.

- **Facilitate training and development**: Training and development provides an incentive for involvement. UCLP is aligning resources by working with the UCLP Staff College to offer patient representatives personal development, including coaching and mentoring.

- **Align resources**: UCLP seeks to align resources across our partners and through engagement with external organisations to maximise value. The partnership’s immediate network encompasses PPI experts based in the NHS, HEIs, BRC/Us, and the CLAHRC. Beyond this UCLP will also work closely with the Patient Experience Action Group, Local Healthwatch Organisations, patient/community groups and third sector organisations, e.g. the London Network of CVS organisations (Community Voices for Health), wherever possible.

- **Increase diversity**: UCLP is committed to ensuring it engages and harnesses the diversity of its population in realising its PPI goals. One initiative is to develop an Online Community of Practice to provide an online forum for our patients to share their ideas. The facility will allow those unable to travel, or with work/childcare commitments to engage. UCLH has also worked with Tribal to develop Microsoft’s Dynamics Customer Relationship Management System into a Patient Relationship Management System to empower young patients to better manage their diabetes and to improve efficiency for clinicians. The software provides an interactive system to allow patients to communicate with their care providers. Initiated in Cancer, we have partnered with BME organisations not just to advise us on research activities, but also to host and deliver BME-specific events to spread word of UCLP’s Programmes and to broaden engagement.

- **Evaluate and Monitor**: Evaluation is essential for successful PPI. Our AHSC Programmes will provide regular reports on PPI and patient and public engagement (PPE) activity to the AHSC Planning and Performance Executive, and interrogate patient experience metrics to inform the research questions which the Programmes address. UCLP has scoped real-time patient experience monitoring at all providers and identified measures of patient feedback that are contributing to value scorecards. UCL is seeking to appoint a Chair in PPI evaluation.

UCLP’s commitment to meaningful patient and public engagement:

We intend for our PPE activity to support our PPI objectives, by encouraging patients, members of the public and other organisations to take an interest in our objectives, and to consider getting involved. To drive this, UCLP has established an active events Programme and UCLP public-facing web and social media, co-designed with patients, as well as increasing national press coverage to build understanding of our aims and achievements.

UCLP also seeks to leverage and integrate the activities of its constituent partners to fulfil its PPI and PPE objectives. For example, QMUL and Barts and The London School of Medicine and Dentistry Centre for Public Engagement, set up in 2012 as part of a Research Councils UK Catalyst award aims to embed and sustain public engagement and support the development of new activity. One such project is the unique ‘Centre of the Cell’ facility (www.centrefothecell.org), a futuristic ‘pod’, dramatically suspended above the laboratories of the Blizard Institute. Visitors experience an immersive mixture of film, digital interactivities and objects relating to biomedical science, intended to inspire curiosity and learning by connecting science to everyday life. Over 150 scientists and clinicians have contributed to its scientific content, which reflects the biomedical research and health priorities of the local East London community. Since the project opened to the public in September 2009, there have been over 69,000 participants in Centre of the Cell activities. From August 2012 to July 2013,169 schools visited the project and 12,880 visitors participated at activities on site, with 5,066 participants in outreach visits to schools and community groups. The UCL Public Engagement Unit is also highly successful, and is one of six UK centres to have been funded by the beacons for public engagement Programme set up by HEFCE, Research Councils UK and the Wellcome Trust. Initiatives include the acclaimed Bright Club ‘comedy nights’ (http://www.brightclub.org), annual UCL Provost Awards for Public Engagement, and annual UCL Public Engagement Symposium.
The track record of the partnership to contribute to economic growth and the economy, including through improved health outcomes and through collaborations with industry:

UCLP’s economic growth strategy acknowledges that ‘health is wealth’. A healthier population provides a larger and more productive workforce and consumer base, which in itself drives the greatest impact on the economy through minimising the cost to the NHS and increasing productivity. The following examples are indicative of our partnerships’ ability to successfully translate discovery science into improved health benefits for the population, driving economic growth:

- Nutrition research at UCL has provided the first experimental evidence in humans that infant feeding and pattern of growth affect long-term risk of obesity and CV disease, leading to major changes in public health and infant nutrition practice.
- Advances at LSHTM in rapid detection of parasite DNA are revolutionising the monitoring of patient outcomes in antimalarial clinical trials, and contributing to maintenance of blood product safety in the UK.
- An evaluation of the reorganisation of stroke care, led by our AHSC partners and others, indicated that over 400 lives have been saved since 2010.
- 2 million pairs of compression hosiery, developed by UCL and distributed under the ‘Saphena’ trademark, are purchased by the NHS every year to safeguard against DVT.

Drivers of wealth gain in the traditional sense include the commercialisation of research. Our AHSC partners’ track-record in this area is extensive, including the formation and spin-out of major companies: (e.g. Arrow Therapeutics, ApaTech, Medic 2 Medic (creators of the ‘Map of Medicine’), Biovex, Stanmore Implants Worldwide, Capteur Sensors Ltd, Biomarin); lucrative licensing agreements: (e.g. Multifyte, Simulect, Activionics Ltd, Stem Cell Treatment for AMD, Virtual Tutor Ltd, Treatment for Hepatic Encephalopathy, Collagen Fabrication, Special Products Ltd, Pentraxin, Ervitech, and Genzon Biosciences); and the creation of novel technologies such as the UCL nanopolymer platform technology, which having passed all its biocompatibility tests to ISO standards, formed the scaffold for the first full human trachea transplant in 2011.

Our member organisations have also developed ongoing and substantial relationships with key industry partners, the promotion and facilitation of which is a key priority for UCLP. Examples of prior success include:

- Barts Health has established a formal collaboration with Quintiles, the world’s largest contract research organisation, as its first “Prime Site” in the UK. Prime Sites receive first notification of all Quintiles trials to be sited in Europe, providing opportunities to researchers and patients to lead/participate in national trials. The company provides infrastructure contributions that support study initiation and recruitment and a commercial management input that helps the Trust to plan for growth and attract more trials to the UK.
- UCL has established a long-term drug discovery and development collaboration with the global pharmaceutical company Eisai. The alliance involves researchers from both organisations working together in new ways to discover novel treatments for neurological diseases such as Alzheimer’s, Parkinson’s and other neurodegenerative disorders. The goal of the collaboration will be to identify and validate novel drug targets, develop new therapeutics and evaluate them in proof-of-concept clinical trials.
- UCL and University of Cambridge have entered a long-term partnership with the Stevenage Bioscience Catalyst SBC leveraging investment from the HEFCE Catalyst Fund (awarded May 2013). The SBC, co-located with GSK, will foster collaboration and interaction between academia and industry and provide an environment to test promising new therapeutic approaches considered ‘industry ready’. UCL has actively engaged advanced biochemical engineering capability in the partnership, and has been successful in receiving NIHR UCLH/UCL BRC funding towards the establishment of 3 projects in the facility.
- UCL has two GSK ‘Discovery Partnerships with Academia’, which are a new approach to early drug discovery, bringing together academia and GSK drug discovery expertise as a joint team to translate innovative research into medicines that benefit patients.
- A major collaboration between UCL and Pfizer - The London Project to Cure Blindness – aims to deliver the world’s first stem-cell treatment for dry age-related macular degeneration (AMD).

The strategy for how the proposed AHSC will contribute further to economic growth and the economy

UCLP’s strategy for future growth focuses on (i) embedding enterprise and wealth generation within the governance structure and ensuring responsibility for enterprise within each Programmatic area, (ii) the promotion of industry engagement with and between our partners, (iii) spreading best practice in research translation and commercialisation across the partnership, and (iv) providing an environment that fosters the generation and diffusion of innovation, complementing the activities of our linked AHSN.

i) Embedding enterprise: Through the establishment of a Wealth Generation Sub-Board, comprised of key players from across the Programmes and representatives from industry and the investment community.

ii) Promotion of industry engagement: UCLP is committed to emulating the partnerships that we have forged (e.g. with Eisai, GSK, Pfizer, Quintiles) with other companies from Pharma and other sectors, particularly
MedTech where we see unprecedented growth and opportunity. We will build on successes illustrated by the multidisciplinary team of biomedical engineers, computer scientists using patient-specific imaging data who have developed the first percutaneous pulmonary valve implantation (PPVI) device (MelodyTM - first FDA approved transcatheter valve device) in collaboration with Medtronic Inc. (Minneapolis, MN, USA).

iii) Spreading best practice in research translation and commercialisation: There is a well-developed and successful research translation and commercialisation infrastructure across the partnership, including UCL Business which supports researchers to identify, manage and exploit IP across UCL, UCLH, RFH, GOSH and Moorfields, and QM Innovations, which provides equivalent support for QMUL and Barts Health. UCL has also established the Translational Research Office (TRO), which supports the translation of UCL’s basic and clinical research into therapies, techniques and medical products with therapeutic value. These aims are achieved through interacting with investigators, identifying translatable opportunities, advising on project progression strategy, accessing suitable funding, and interfacing effectively with potential industry partners. Since its inception in 2009 the TRO has built and manages a translational portfolio of over 30 projects with a combined research value of £40m. The TRO has also taken a lead in the establishment of major biomedicine partnerships with industry, such as the Eisai and Stevenage Bioscience Catalyst described above.

In spanning both the NHS and academia, UCLP acts as a facilitator to drive commercialisation. UCLP is encouraging the creation of ‘NHS Partnership Managers’, to facilitate bidirectional interaction in the HEI partners and NHS Trusts (Moorfields post already appointed, GOSH appointment imminent). These Managers will build upon the successful Translational Research Office model at UCL targeting funding that promotes this agenda and reducing duplication of effort across a large partnership.

iv) Fostering innovation: UCLP will strongly focus on embedding a culture of innovation and knowledge exchange, specifically i) addressing the education of patients and populations in self-management; ii) educating and training scientists to be more aware of commercial opportunities that may evolve from their research; iv) working closely with SMEs to incubate budding entrepreneurs through access to our network of skilled and experience professionals; v) assessing the feasibility of a physical UCLP Innovation Centre as a way to encourage scientific or clinical spin out companies to evolve.

**Our plans for measuring our contribution:** Each of our AHSC Programmes will be required to provide clear metrics on their enterprise activity, including job creation, patents, trademarks, licensing agreements, and investments. In addition to more traditional metrics, we will seek a more innovative approach to the measurement and evaluation of economic growth (working with CASMI), encompassing the value of knowledge transfer, enhanced patient outcomes, increased quality of life, improved workforce productivity, and increased collaboration which drives creative thinking. Through collaborative knowledge exchange we aim to focus on understanding the nature, extent and processes involved in the return on investment in medical research, by applying a more holistic and academically driven approach. It is hoped that this will benefit our own strategic prioritisation of resource, and also inform a broader understanding, informing the London-Oxbridge ‘MedCity’ development and national Wealth Generation agenda.

The plans and strategy for identifying, managing and exploiting IP, including the track record of patents filed and granted, spin-outs and income generated from commercialisation of assets.

UCLP recognises the strength of the Technology Transfer infrastructure of our partner institutions and their established track record in managing and exploiting IP.

- Over 2008-09-2012/13, UCL Business has facilitated 228 patents to be granted, the spinout of 124 companies, 100 licences and income of £24.7m.
- QM Innovations has facilitated the filing of 189 patents, 38 patents granted, 3 new spinouts and spinout investment of £45m, and commercial income (licence and spinout exits) of £11.7m.
- LSHTM’s Chariot Innovations Limited aims to help researchers achieve greater impact from their project by making it easier to access users. The School’s Intellectual Property track record includes 95 Patents filed, 9 granted, 1 spin out company formed and income generated of £85,000.

Examples of our successes include:

- Biovex was founded in 1999 and developed a portfolio of cancer destroying medicines based on herpes simplex virus research. The company was sold in 2011 for $1bn to Amgen Inc, California.
- ApaTech, an orthobiologics company specialising in synthetic bone graft materials spun-out from QMUL in 2001 was acquired by Baxter International in 2010 for a total consideration of up to $330m.
- The Retroscreen Virology Group, based in the QM BioEnterprises Innovation centre, pioneered the commercialisation of the Viral Challenge Model (VCM) to accelerate and reduce the cost of bringing antiviral therapeutics and vaccines to market. RVG listed on AIM in 2012, raising £15m, and in May 2013 raised another £25m to drive the next phase of the business.
- UCLP sees its key role as being to facilitate sharing of best practise that has enabled the successful track record described, and crucially to consider the barriers to success and shared learnings from apparent “failures”. Our aim thereby is to create a more unified and streamlined approach to IP and its exploitation across our AHSC partnership, driven through our Wealth Generation Sub Board
### 8. STRATEGIC PARTNERSHIPS & WORKING WITH NIHR-FUNDED RESEARCH INFRASTRUCTURE (2 pages)

#### Detail of the proposed AHSC’s strategy for building meaningful external partnerships including:
- The strategy for linking with NIHR-funded research infrastructure, e.g. Biomedical Research Centres or Units, CLAHRCs, Healthcare Technology Cooperatives, Diagnostic Evidence Cooperatives and Clinical Research Network;
- Other existing strategic partnerships, and the strategy to develop new partnerships, that will enhance the delivery of the proposed AHSC’s objectives.

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<th>UCLP’s strategy for building external partnerships including NIHR-funded research infrastructure</th>
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<td>UCLP’s overarching purpose is to effect population health and wealth gain through the effective translation and diffusion of research that addresses societal need. Our AHSC strategy for realising these linked objectives recognises that impactful science is promoted by interdisciplinarity, inter-institutional collaboration and close links with industry (RAND Analysis, 2013). We also recognise the need for commitment to each link in the translational chain, much of which is provided by NIHR infrastructure. In addition to its status as an AHSC and AHSN, UCLP serves as a framework to engage and align the activities of three NIHR BRCs and two NIHR BRUs and a new Local Integrated Comprehensive Research Network, (a principal focus of our AHSC activities) and link with an NIHR CLAHRC and a Health Technology Cooperative.</td>
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Our strategy for alignment and integration is facilitated by:
- A common culture of partnership working that is primarily responsive to patient need, and shared values that emphasise our primary purpose (population health and wealth gain), academic excellence, and service pathway integration that draws on relevant academic expertise across the translational spectrum. Strong links exist between the BRC/Us to promote sharing of best practice, economy of scale supported by common metrics which the AHSC promotes. The Central and East London CLRN is regularly in the top three CLRN’s in the UK for patient accruals, with a high proportion coming from complex studies and has taken a lead role in developing the new local Integrated Comprehensive Research Network (ICRN), now nationally commissioned as a learning experience. Metrics are received by the AHSC Research Sub-Board monthly. The AHSC also enjoys an active dialogue with the NIHR Clinical Research Facility at UCLH/UCL and the NIHR CLAHRC, awarded in August 2013 which will undertake high-quality applied health research focused on the needs of patients, and evidence implementation into practice.
- Integrated governance: The cross-cutting AHSC Sub-Boards bring together Senior Leaders from across the NIHR funded infrastructure to ensure alignment of strategic objectives. For example, the Research Sub-Board includes the Directors of the Biomedical Research Centres and Units, the Central and East London CLRN, CLAHRC, AHSN and HEIs, and ensures the development and delivery of an aligned research strategy (from experimental through to applied research) and common barriers to translation can be identified and addressed. Further integration is assured at the AHSC Planning and Performance Executive involving Programme Leads and Sub-Board Chairs and ultimately governed by the UCLP Board to which the AHSC, AHSN, CLAHRC and CLRN report.
- Aligned Programme strategies: Our AHSC Programmes are synonymous with our BRC/U Programmes recognising the critical step in translation these organisation play and our evident strengths in those areas. Our AHSN Programmes broadly align and our integrated structure enables close dialogue to foster transmission of the outputs from our AHSC. The CLAHRC with which we are engaged exhibits similar alignment, the generic learning on implementation informing all Programmes.

The linkages and commitment to the whole translational pathway are represented in the below figure which also illustrates the integration with other critical strategic partners, including the Francis Crick Institute, due to open in 2015, the LETBs, NICOR and PHE, and the Farr Institute @ UCLP (underpinning informatics and the identification of health risks).
Other existing strategic partnerships and the strategy to develop new partnerships that will enhance the delivery of the proposed AHSC’s objectives.

Given that effective partnership working is core to our philosophy we actively seek external partnerships that:

i) are consistent with our values, ii) align with our purpose, iii) offer complementary strengths and add value.

Conscious of the major changes occurring in the pharmaceutical industry reflecting limitations of the historic drug development process we are forging major constructive partnerships that draw in particular on our expertise in fundamental science, proof of concept and clinical trials. The links are more fully addressed in Section 7, but a measure of our activity in this area is UCL’s status as the institution with the greatest number of such partnerships in the UK according to a Nature survey in 2013 (Nature Biotech, 2013, Vol.31, 383).

London, Oxford and Cambridge:

- UCLP has built on UCL’s founder partner status in the Francis Crick Institute and has pioneered a process of academic engagement with other partners. Most recently UCLP in conjunction with UCL, QMUL and the Francis Crick Institute (together with the Sanger and European Bioinformatics Institute) have submitted a major joint bioinformatics bid after a competitive shortlisting process.
- London-wide, UCLP also precipitated and continues to provide secretariat support to the London AHSC Executive, which helps to integrate the activities of the three London AHSCs (See Section 9).
- UCLP has championed engagement with the Oxford and Cambridge as well as London AHSCs to better project the UK’s core strengths in Life Science. UCL/UCLP sponsored a GMEC Rare Diseases initiative involving UCL, QMUL and the four other GMEC centres leading to novel industrial partnerships.
- UCL also formed a joint Institute with Oxford University – CASMI – the Centre for the Advancement of Sustainable Medical innovation (CASMI http://casmi.org.uk/) – to address in an holistic fashion the many barriers to economically sustainable drug discovery ranging from better appreciation of patient need, more sophisticated ways of determining proof of concept and predictive toxicology, through to adaptive licensing, economic evaluation, adoption, diffusion and ultimately adherence.
- With Cambridge, UCL has recently received a HEFCE Catalyst award for engagement with the Stevenage Bioscience Catalyst, providing co-located industry expertise (see Section 9).

National:

- National outreach and engagement is a strategic priority for all of our BRCs. Illustrative strategic links include: the joint MRC Centre in Neuromuscular Disease, an experimental medicine initiative between UCL, UCLH/UCL BRC, GOSH/UCL BRC and Newcastle; Moorfields Institute of Ophthalmology BRC and Bristol University linkages relating to inflammatory eye disease; GOSH/UCL BRC hosts the Rare Disease Translational Research collaboration for Immunology collaborates with the Sanger Institute on UK10K
and the Deciphering Developmental Disorders Programme, and links with the NIHR Cambridge BRC as part of the NIHR's Bioresource BRIDGE Consortium.

- We have played a leadership role in the development of the AHSN model, visiting and advising most of the 14 emergent AHSNs, and in supporting the “Network of Networks”.

- We are hosts to a number of major Cohort studies, for example the MRC/ESRC funded Life Study assessment centre between the UCL Institute of Child Health, North East London Foundation Trust, PHE and NHS England will track the growth, development, health, well-being and social circumstances of around 100,000 babies and their families. This UK-wide study will provide a rich and internationally unique longitudinal resource of data, environmental and biological samples that can be used to address future questions and hypotheses regarding early life origins of disease, health and development.

International:

- Barts Health has established a formal collaboration with Quintiles, the world’s largest contract research organisation, which established Barts as its first “Prime Site” in the UK.

- The Yale: UCL transatlantic collaborative explicitly involves UCLP and has fostered exchange of specialist expertise in the fields of sudden death syndromes and device development. A joint CV device development initiative has begun with UCLP leading the human trials.
9. WORKING WITH THE NHS ARCHITECTURE (2 pages)

Please describe the proposed AHSC’s strategy for engaging with the wider NHS architecture including:

- The strategy for ensuring that:
  - the AHSC is fully nested within the relevant local AHSN;
  - there is integrated working with the local AHSN, emphasising the complimentary roles of AHSCs and AHSNs;
  - there is appropriate co-working with other AHSNs nationally to deliver improved outcomes for patients and the NHS.
- How the proposed AHSC will engage with primary, secondary and tertiary care sectors, NHS commissioning organisations and social care providers to improve outcomes for patients;
- How the proposed AHSC will work with other AHSCs to improve outcomes for patients and the NHS.

The AHSC is fully nested within the AHSN: Our operating model goes beyond the requirement for the AHSC to be fully nested in the AHSN. We believe we are the only AHSC in the UK to completely integrate the two functions into a single health science system whilst ensuring clear accountability for the 'conventional' AHSC function. We have always believed as an AHSC that we could only realise our purpose of accelerating medical advance and its diffusion for the benefit of the population's health and wealth through establishing a genuine partnership with our broader health community and the diffusion mechanisms now characterised as AHSN functions. This fully integrated partnership model which is core to our philosophy has taken more than four years to build, initially involving partners in North Central London, then expanded into North East London in 2011, covering a population of 3.2 million.

As an accredited AHSN UCLP has extended its reach and impact to engage much of Essex, West Herts and South Beds, sub-serving a total population of over 6 million and involving more than 100,000 healthcare professionals. We see the following fundamental advantages in an AHSN of such scale and integration in delivering our AHSC agenda: i) all of our activities are grounded in those issues of real importance to our population that reflect the major contemporary health challenges and the need for preventative strategies rather than adopting a solely 'hospital-centric' perspective; ii) the breadth of the partnership provides the healthcare educational expertise to prepare the whole workforce; and iii) the impact of our partnership is amplified, involving as it does almost 10% of the UK population. The effort expended in establishing this framework, allowing population-wide access and impact, enables our AHSC to focus on its core functions in pursuit of its purpose, confident that the mechanisms for the diffusion, implementation and relevant service integration are firmly in place.

Close integration with our AHSN that recognises the complementary roles of the AHSC and AHSN is fundamentally underpinned by sharing a common purpose and reinforced by our integrated governance arrangements. The AHSC and the AHSN are supported by a single not-for-profit company governed by a single UCLP Board. A single Managing Director, Academic Director and COO, facilitate integration and partnership working and oversee delivery of the complementary agendas. The various Programmes report to the Board with reference to the UCLP Chief Executive Group which involves the heads of all of the organisations that are part of the AHSC and/or AHSN to ensure effective engagement with our integrated approach. Perhaps most importantly, the commitment to a common purpose and the engagement structures established prior to AHSN status, together with an evident commitment to partnership working, have fostered a profound shift in culture. Partners are more willing to entertain developments that bring system advantage for the benefit of patients and engage in the wealth creation agenda. Considerable effort is expended by the leadership in developing and sustaining that culture through regular personal contact and attending to business of deep concern to NHS leaders, as well as the formal mechanisms of governance. That culture, fostered by our UCLP since inception, has enabled our AHSN to become established more rapidly and register considerable early achievement (see our ‘100 day plan’, http://www.uclpartners.com/lotus/about-us/our-100-day-plan/). It has also facilitated the development of our associated CLRN, LETB and CLAHRC, each of which in turn reinforce the same shared ethos at different points along the translational spectrum.

Committing with other AHSNs nationally to deliver improved outcomes for patients and the NHS

We are proud to have played a leadership role in the development of the AHSN model, drawing on our experience described above. Throughout the AHSN development process we shared our thinking (and prospectus) with emergent AHSNs and engaged with most such organisations. We have subsequently played a leadership role in supporting the “Network of Networks”, actively facilitating wider diffusion of innovation.
How the AHSC connects the AHSN and to the broader health and social care environment to improve patient outcomes: Our integrated governance arrangements, Chief Executives Group and focus on our primary purpose ensure the required connectivity. The effectiveness of such arrangements is best illustrated through the specific example of research-informed mental health provision. Fundamental neuroscience leading to diagnostic and therapeutic innovation that will be amplified by the proposed AHSC’s neuroscience workstream informs the AHSN mental health Programme of emerging opportunities. The AHSN mental health Programme hosts the network of Clinical Commissioning Group Mental Health leaders that includes all 32 CCG leads from across London, in collaboration with the Mental Health Strategic Clinical Network (SCN). This network is being extended to include south Essex, Herts, Luton and Bedfordshire. London SCN and UCLP have partnered to launch a pan-London network through which improvement and re-design work can be co-ordinated. UCLP has been asked to lead on the development of the dementia value scorecard for London on behalf of the London AHSNs, SCN and NHSQI Dementia network. The evaluation of specific initiatives and effective implementation will be supported by the newly established CLAHRC, which embraces a mental health theme and will bring together applied health researchers and implementation scientists to that end.

Nationally, the Mental Health Programme has partnered with NHS England and many other local and national leaders. For example, Prof Geraldine Strathdee, National Clinical Director for Mental Health who is a visiting professor at UCL, holds a leadership role in the UCLP Programme as the Director of Professional Education. Through such links, we have started to promulgate such activity across the national AHSN/SCN Mental Health network.

How the proposed AHSC will work with other AHSCs to improve outcomes for patients and the NHS

We have since 2010 championed close collaboration between the three London AHSCs, precipitating the formation and providing secretariat support to the London AHSC Forum, now Executive, which also embraces the new AHSNs. We also led the formation of Improvement Science London, building research capability across the three AHSCs to tackle issues relevant to the whole London population. Together with our London partners we have collaborated on a London Life Sciences initiative supported by the GLA which aims to link therapeutic discovery potential in London (plus Cambridge and Oxford) and better project such capability to secure inward investment and industrial engagement. We plan that this development will integrate with the Mayor’s plans for MedCity, promoting the South East AHSC cluster as a biomedical power base.

As a partner within GMEC we have sponsored a rare diseases initiative involving all six centres that is on the verge of striking a contractual relationship with a major pharmaceutical company to develop new therapies for those conditions.

We have worked closely with the University of Cambridge, leading the successful HEFCE bid to resource the initiative, and Cambridge Health Partners to establish ‘industry ready’ therapeutic development projects within the Stevenage Bioscience Catalyst. We see this as part of a broader collaboration with Cambridge University and AHSC to build the ‘M11 corridor’ as a key axis for biomedical discovery and its translation.

As outlined in Section 8 we are partners with the University of Oxford (and AHSN) in CASMI, the Centre for the Advancement of Sustainable Medical Innovation, which seeks to address the issues that have led to current failures in the translation of basic bioscience into affordable and widely adopted new treatments. Moving forward we will actively engage with the designated AHSCs and other UK centres with niche excellence and international equivalents to foster inter-institutional collaboration and networked capacity building. We believe our partnership credentials and founder partner status in the Francis Crick Institute provide us with the opportunity to foster such alliances to drive impactful research for the benefit of NHS patients.
10. INTEGRATION OF RESEARCH, HEALTH EDUCATION AND PATIENT CARE (3 pages)

Detail of the proposed AHSC’s strategy over the next five years for furthering integration of research, health education and patient care including:

- Evidence that the partnership’s ability to translate discoveries from basic science into excellent translational, clinical and applied research, and into benefits for patient health and improved health outcomes. Please provide 5 examples from over the past 5 years;
- A description of how the partnership will achieve further integration of research, health education and patient care over the next 5 years as an AHSC;
- How this increased integration will lead to improvement in research, health education and patient care;
- The partnership’s vision and strategy for maximising the impact that multi-disciplinary and multi-professional working across the AHSC;
- Details of the partnership’s close working with the LETB and how this will further the aims of the AHSC.

Five examples of partnership’s ability to translate discoveries from basic science into excellent translational, clinical and applied research, and patient benefits and improved health outcomes:

Accelerating the translational process into substantive health benefit is a major strategic aim of our AHSC. The five examples selected, exemplify our commitment to the whole translational pipeline.

i) Multiple Sclerosis: UCL/UCLH have combined their large patient population and expertise in rapid imaging, pathology and service innovation with QMUL’s expertise in epidemiology, immunology, pathology and genetics to create one of the largest centres globally for multiple sclerosis research and clinical practice informed by leading edge PPI (see www.shift.ms). Over the last 18 months this initiative has been awarded £11.3m in joint grants. Current research includes: (i) The evaluation of Canbex, a cannabinoid analogue, from basic science through first in man studies (N Engl J Med, 2006, 354, 899-910) and from 2013 a Phase 2 trial; (ii) Innovation in adaptive investigator-led trials, for example the MS SMART trial (with four arms trialling three neuro-protective agents for Progressive MS, vs. one control) beginning autumn 2013. Innovative clinical services have been developed which form the basis of NICE guidance that is being diffused across the partnership. The clinical workforce is prepared to adopt such innovative practice through the creation of an MS preceptorship, with 2-day courses available for all clinicians who work with MS patients.

ii) Amyloidosis: Professor Sir Mark Pepys FRS has invented new therapies for amyloidosis, type 2 diabetes, Alzheimer’s disease, CV and inflammatory diseases, with >15 patents held by the UCL spinout company, Pentraxin Therapeutics Ltd. GSK initiated their current approach to drug discovery partnerships with academia by licensing his key patents in 2009/10, and GSK are collaborating closely in their development. Initial patient studies of the first in class small molecule/humanised monoclonal antibody combination for elimination of amyloid deposits (Nature, 2010, 468, 93-97), started in June 2013. The UCLP component of the GSK collaborations is conducted in the Wolfson Drug Discovery Unit of the UCL Centre for Amyloidosis and Acute Phase Proteins. The UCL Centre at the Royal Free also includes the NHS National Amyloidosis Centre to see the national caseload of systemic amyloidosis (>3000 patients per year) and familial periodic fever syndromes.

iii) Trachoma: LSHTM’s research on trachoma, the leading infectious cause of blindness, has shown that a single oral dose of azithromycin is an effective, feasible mass treatment and could eliminate trachoma from affected communities.RCTs conducted in various African settings demonstrated the efficacy of this approach at scale. In 2008, with Gates Foundation funding, a partnership was established for the rapid elimination of trachoma, comparing the impact and cost effectiveness of different strategies for the administration of azithromycin. This work has been life changing for millions of people in communities affected by trachoma and led to Pfizer donating azithromycin (when still under patent) to trachoma control Programmes in eight countries, subsequently increased to 21. Since 2008, 205 million azithromycin doses have been donated. WHO elimination targets have been achieved in 9 countries.

iv) B-cell depletion in rheumatoid arthritis (RA): Research at UCL pioneered B-cell depletion to treat RA and stimulated the development of B-cell-directed therapies for other autoimmune rheumatic, haematological and neurological diseases. Now NICE approved (in 2007 updated for 2011), B-cell depletion (based on rituximab) in RA is as effective as the alternative (anti-TNF drugs) and allows effective treatment for patients unable to gain benefit from anti-TNF drugs. Rituximab offers cost savings of up to £5,000 patient and is a more convenient, being given as an infusion at approximately six monthly intervals. B-cell depletion has also proven to be safe, with many receiving repeated courses of treatment. By mid-2013 an estimated 230,000 patients have been treated with rituximab for RA.

v) Gene Therapy: Research at the UCL ICH led clinical trials of gene therapy for primary immunodeficiency diseases at GOSH. These I trials have offered successful treatments to children for whom there was little chance of "cure" by the only other possible means, haematopoietic stem cell transplantation Initiated in 2002 for SCID-X1, 32 patients have been treated for four different primary immunodeficiency disorders, which is
comparable to the other major world centre in Paris. The total number of patients treated to date are: 12 patients with severe combined immunodeficiency (SCID-X1), 13 patients with adenosine deaminase deficient severe combined immunodeficiency (ADA-SCID), 5 patients with chronic granulomatous disease (CGD) and 2 patients with Wiskott-Aldrich syndrome (WAS). The majority of treatments are successful with the patients now at home leading active lives.

A description of how the partnership will achieve further integration of research, health education and patient care over the next 5 years as an AHSC:

Research integration will be advanced through recognition and promotion of synergistic and a profound commitment to interdisciplinary and inter-institutional working, evidenced by UCL’s highly successful ‘Grand Challenges’ now emulated by many Universities and pan-Faculty research domains. Integration will be reinforced by AHSC Programme Steering Groups involving members drawn from strengths across the AHSC and the full translational spectrum. The Research Sub-Board oversees a collective approach to overcoming barriers to translation and receives reports from BRC/Us, CLAHR and CLRN.

Education integration is facilitated by close working with the local LETBs (see final sub-Section). UCLP is contracted to act as lead provider (the largest in London) for a comprehensive range of postgraduate medical and dental education Programmes. Supplementary multidisciplinary Masters level modular provision draws on expertise across the academic partners. As with research, the Education Sub-Board, upon which our LETB representatives sit, ensures Programmes are aligned and appropriate inter-professional opportunities seized. Generic issues e.g. recruitment of trainees with the right attributes are overseen at this level.

Integration of patient care will be advanced through further development of integrated pathways of care (see below) and a range of quality and value enhancement initiatives drawing on the Partnership’s Care Quality Sub-Board and Forum, benefiting from our strong collaboration with Partners Healthcare in Boston USA.

The integration of all three components will be facilitated by the following means:

- The research agenda will be informed by unmet care needs drawing on healthcare outcome measures, our PPI Programme and input from the CLAHR and the UCLP Chief Executives Group.
- We will proactively consider the research and educational implications associated with major service development. Liaison groups will be formed between Trust and AHSC academic leads to secure joint strategic objectives, aligning as appropriate capital Programmes, staffing and philanthropic effort.
- The relevance of our educational Programmes to care needs will be assured through the development of patient informed curricula and involvement of ‘expert patients’ as teachers.
- Our informatics Programme platform (see Section 4) will jointly address research and care needs.
- The Research, Education, Wealth Generation and Care Quality Sub-Boards will report to the AHSC Planning and Performance Executive which is charged with overseeing appropriate integration.

How integrated will lead to improvement in research, health education and patient care:

We see service pathway integration, drawing on best research evidence and a critical mass of specialist and academic expertise, as key to achieving world-class outcomes. UCLP has brokered such service ‘rationalisation’, applying these principles to cancer and CV services, and increasingly to mental health:

- **Our Cancer Programme** (“London Cancer”) is at the forefront nationally in making step-change improvements in care. As a strong integrated provider system, it works to optimise patient outcomes and experience across the whole pathway for 11 tumours. Each pathway is led by a clinical academic or NHS consultant linked to QMUL or UCL increasingly supporting and challenging each other to reduce variation and work as one system, using the benefit of single sites and teams for highly specialist interventions. Research (bench, applied, epidemiological, behavioural and qualitative) is key at all stages, facilitated by the merged clinical research networks. Benefits include an expanded, coordinated portfolio of research; in brain cancer, for example, trial recruitment has doubled since 2011. Moving forward the outputs from our proposed AHSC Cancer Programme with its personalised medicine focus, supported by our commitment to Informatics, and prevention-orientated lifelong health initiatives will add further value.

- **Our Cardiovascular Programme** builds on experience from a successful reorganisation of stroke clinical services, focusing hyper acute stroke care at three sites compared to twelve and reducing 30 day mortality from 12-30% to <10%. Subject to public consultation, existing CV services within UCLH will move to a new-build heart centre at Barts. This will be the “hub” of an integrated system, with joined-up primary care and local hospital-based networks, and an integrated academic strategy building on UCL and QMUL complementary expertise. The vision for the centre was co-created by over 100 clinicians, researchers, patients and other stakeholders. The new hub and system will provide a test-bed for novel devices emerging from academia. As such the AHSC’s Cardiovascular Programme (Prevention, pharmacotherapy, and devices) as well as lifelong health initiatives will fuel further advance.

- **Our Mental Health Programme** brings together leading mental health researchers from UCL and QMUL, a London wide network of mental health leads from CCGs and the six NHS provider MH Trusts in UCLP’s AHSN. Key themes, covering the entire age span and pathway of care, include designing resilience building Programmes (in collaboration with PHE), designing MH interventions to support employment; and
the integration of mental and physical health with the aim of creating sustainable systems for improving value in the delivery of mental health outcomes. The patient experience has been improved by implementing shared decision making in dementia services, across seven sites. Our education Programme has trained 2,000 acute and mental health trust NHS staff in dementia and we are currently training a further 12,000 NHS staff in dementia awareness. We have a national leadership role to improve mental health services for children involving training staff in recent advances in evidence-based therapies. We also focus on reducing premature mortality in people with mental health disorder through reducing CV risk.

The same integrative approach will be adopted for the remaining AHSN Programmes (Co-Morbidities and Maternal, Child & Adolescent Health), and specialty-specific initiatives.

The partnership’s vision and strategy for maximising the impact of multi-disciplinary and multi-professional working delivers across the AHSC:

As described above, UCLP sees the value of a multidisciplinary perspective as pivotal to rapid scientific advance and innovation. Our commitment to multidisciplinarity is evidenced by an external stakeholder analysis for UCL, which identified multidisciplinarity and inter-institutional collaboration as key distinguishing features (Echo Research, 2012). Since 2010, UCL has also championed the development of fluid research ‘domains’ that extend across the institution, and beyond, bringing together expertise from a variety of backgrounds to focus on particular challenges, an approach that led to the award of the Sainsbury Wellcome Centre for Neural Circuits and Behaviour, and the Wolfson Centre for Experimental Neurology, both due to open in 2014 and, more recently, the MRC EHIRC and Farr Institute @ UCLP.

In developing such multidisciplinary fora, we are conscious that contemporary health problems will not be solved through biomedical science alone. For example, medical device innovation requires close working with the pan-Faculty UCL Institute of Biomedical Engineering, London Centre for Nanotechnology (joint with Imperial College London); and the Yale-UCL Collaborative CV devices initiative.

The formation of CASMI, joint with University of Oxford, recognises that a constellation of world-class excellence in law, ethics, economics and behavioural science as well as the biomedical disciplines is needed if the innovation pipeline is to be optimised in a holistic fashion.

Our strategy moving forward builds on the successes of the UCL research ‘domains’. All our Programmes and cross cutting initiative in informatics, personalised medicine and lifelong health will engage interested academics across all disciplines, partners and beyond. Links will be fostered by Town Hall meetings, ‘speed-dating’ initiatives, workshops on emergent opportunities and bids. To facilitate such activity we will enhance our team of highly skilled Research Coordinators to ensure support each Programme.

Effective functional team working is key to optimising clinical outcomes. Given the multi-professional nature of contemporary teams, attention to role definition and development, team working and leadership are critical to our success. We acknowledge that many attempts to promote inter-professional activity have been disappointing. Rather than treating all students the same, we focus on ensuring undergraduate students understand their roles and those of the healthcare team through joint placement activity focused on real world clinical issues. Our multi-professional Programmes provide skills that are generic to all professions e.g. research training, educational skills, service improvement, management and leadership.

Our strategy moving forward will extend further such Programmes and establish multi-professional learning sets that will work together in their clinical setting to foster the right skills, attitudes and behaviours. In the academic field we will foster ‘team science’ and award an annual ‘UCLP Team Prize’.

Details of the partnership’s close working with the LETB and how the aims of the AHSC will be furthered:

UCLP facilitated the formation of the Health Education North Central and East London (HENCEL) LETB, UCLP’s MD chairing its Development Board. UCLP is also actively engaged with the East of England LETB, which together with the HENCEL covers our AHSN. UCLP acts as lead provider for commissioned health care professional education Programmes across NC and E London including around 40% of Postgrad Medical Education and Training for London. Examples of partnership working include:

- Galvanising support from the LETBs to sustain clinical academic training capacity in our specialist centres, key to the AHSC mission;
- Quality Improvement fellows working across both the LETB and UCLP to support improvement skills training and development across the partnership;
- The LETB has invested £650,000 in 2013 in UCLPartners to deliver 3 strategic educational Programmes to improve health outcomes in child health, quality improvement capability and mental health;
- Co-developing strategies to inform inter-professional education and the appropriate adoption of digital education solutions and simulation technologies.

The Chair of the HENCEL LETB sits on the UCLP overarching Board, which has the overall remit of integrating the activities of our AHSC, CLRN, AHSN, CLARHC and education providers.
Please describe the current and prospective financial performance of the partnership’s constituent NHS provider and university organisations.

HEI and NHS Partners’ Financial performance: The collective annual turnover of the partners is in excess of £4bn. Despite austerity across the public sector, our partners are strongly placed to resource the delivery of internationally competitive research, teaching and patient care due to the flexibility provided by multiple income streams and a strong asset base. Set out below, by sector, is a high-level summary of the partners’ current and prospective financial performance. The combined income of the charities affiliated with our partner Trusts was £103m in 2011/12, 7 times greater than that of any other London AHSC, on an asset base of £626m. Private patients’ income within our Trusts exceeds £68m, for example 11% of Moorfields’ total turnover is derived from private patients. In addition our partners own central London property portfolios worth around £4bn.

University Organisations (University College London (UCL); Queen Mary University of London (QMUL); The London School of Hygiene and Tropical Medicine (LSHTM))

The three Universities are forecasting an operating surplus in the current financial year (2012-13) and are planning surpluses over the next 4 years. UCL has delivered a surplus in all years since the inception of UCLP (a retained surplus of £26m in 2011/12) and is expecting income to be over £1bn for the first time in 2013-14, with a continuing upward trajectory in the following years. LSHTM delivered a surplus of £1.8m against total expenditure of £113m in 2011/12. The surplus for 2012/13 is likely to be in the region of £2.5m. Whilst QMUL reported a deficit in 2011-12 this was mainly due to the changing nature of student funding and significant investment in IT improvements. The university is forecasting a surplus in 2012-13 of approximately £9m due to successful initiatives in cost control and an additional year of students subject to the new funding regime. The three universities are responding to an increasingly competitive research-funding environment and a growing global competition for students. All organisations are looking at significant investment over the coming years to secure and increase student numbers through optimising their educational programmes and student experience, enhancing their infrastructure (estate and IT), appointing globally high calibre academic staff and developing commercialisation of research activity.

NHS Organisations

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All the NHS Foundation Trust organisations achieved a Monitor Financial Risk Rating (MFRR) of 4 in 2012-13 and most are forecasting 4 for at least the next three years (as per their Monitor Plan submissions). UCLH are forecasting a reduced MFRR of 3 as they expect surpluses to be modest, around £2m on a turnover in excess of £800m, due to significant efficiency requirements, capacity constraints with regard to increased demand. The Barts Health Trust Board approved a turnaround plan to deliver improvement in the financial standing of the organisation over the next 2-3 years. The Trust is committed to delivering a successful turnaround Programme and is focused on making month on month improvement to year-end. The NHS TDA will “hold the trust to account for delivery of its financial plan and this in turn will ensure that the trust is viable in the medium to long term and can make progress to FT authorisation (Source: Alwen Williams, NTDA). All of the NHS organisations are committed to continued delivery of efficiency requirements (ranging from 4% to 8% year on year) and development of new income streams (e.g. international growth strategy at GOSH; development of Proton Beam Therapy and reconfiguration of specialist services at UCLH and new central facility for integrated care, research and education at Moorfields).

UCLP Financial performance: UCLP, a not for profit company, has achieved breakeven since its incorporation. Its forward three-year plan is to continue to breakeven. The Partners have agreed to provide £500K from their contributions to support senior managers in the operational delivery of the AHSC including the research co-ordination of the six Programmes. In addition to these direct financial contributions to the AHSC each AHSC partner provides salary support for their clinical academic leaders in their AHSC roles.
Please use this section to address directly any feedback provided by the Panel on your application at the shortlisting stage, including any highlighted issues with quality of patient care such as adverse Monitor or CQC ratings.

Further information on the balance between number of organisations and geographical size, with the ability to achieve the close working, alignment and strong governance to deliver our aims.

The depth of expertise required to deliver world-class clinical, research and educational outcomes is leading to increasing institutional specialisation, particularly in our part of London where for historical reasons, separate world-class specialist hospitals with associated postgraduate medical institutes developed, merging with UCL between 1994 and 1997. Moorfields/UCL’s Institute of Ophthalmology, Great Ormond Street Hospital/UCL’s Institute of Child Health, and UCLH’s National Hospital for Neurology and Neurosurgery at Queen’s Square/UCL’s Institute of Neurology have been highly successful since incorporation and host the ‘centre of gravity’ for three of our six AHSC Programmes. We intend to build on that successful model by investing in specialist services and academic development at the Royal Free in Immunology and Transplantation, contributing in a major way to our III Programme, Cancer at UCLH, and CV at Barts Health/QMUL, integrating with complementary strengths at UCLH/UCL. Geographically, these AHSC Centres are located within a radius of three kilometres, with UCLP’s offices acting as a central hub for the specialist sites.

Since submitting our PQQ, we have reformatted our Programmes to reflect these structures, current developments and the immense opportunities they present to achieve genuine world-class status in all of our endeavours. We do so however without losing sight of the prospects offered by supporting underpinning cross-cutting initiatives in personalised medicine, lifelong health and informatics where we believe major prospects for advance reside over the next five years and where we have excellent collective capability. We will use the highly successful ‘research domain’ construct developed by UCL over the last four years, networking multidisciplinarity interests in these areas across the partnership, to the benefit of all Programmes. Given the centrality of informatics to future success, we have established a Sub-Board chaired by the National Director of the Farr Institute of Health Informatics Research to drive this agenda.

By reformattting our Programmes in this way, we maintain we have created a simple, clear structure to govern the AHSC that optimises alignment with our BRCs/Us, and other parts of the translational pathway, with clear accountability at all levels. We have achieved this whilst maintaining the connectivity with our broader health community, the UCLP main Board serving to coordinate the activities of our AHSC, AHSN, CLAHRC and CLRN and promote alignment whilst being the guardian of our values and commitment to genuine partnership working. The model that has been created facilitates societal engagement and delivery at unprecedented scale.

The Panel noted the quality and safety concerns at the Newham and Whipps Cross sites of Barts Health. The TDA, UCLP and others are supporting Barts Health leadership and staff to address these, our own involvement reflecting UCLP’s profound commitment to quality improvement initiatives since inception e.g. the deteriorating patient initiative achieving 33-45% reduction in cardiac arrests in participating Trusts in the last two years, and the UCLP Quality Forum with >95% attendance.
13. DECLARATIONS AND SIGNATURES

By signing the declarations the named individual is agreeing that they are authorised to do so on behalf of their organisation.

Please print this page, have it authorised and return it by post by 7 October 2013 to the address stated at the bottom of this form.*

The applying English NHS Provider/University Partnership fully endorses the application for an Academic Health Science Centre award and assert that appropriate support will be provided to the AHSC should the application for designation be successful.

English NHS Provider/University Partnership: UCL Partners........

Name, job title, address, email and telephone number of the lead contact for the proposed AHSC:
Professor Sir John Tooke, Vice Provost Health and Head of the School of Life and Medical Sciences UCL and Academic Director, UCL Partners.

Address: UCL, Gower Street, London WC1E 6BT
Email: j.tooke@ucl.ac.uk
Tel.No. 020 7679 0878; Mobile 07778 607440

Signature ........................................... Date: ..........30 September 2013..............

(Lead contact for the proposed AHSC)

If you have questions about the completion of this form please e-mail Sonja Tesanovic at sonja.tesanovic@nihr-ccf.org.uk.

This form must be submitted by 1:00pm on 30 September 2013. The 'wet-ink' Declaration and Signatures section of the application from should be received by NIHR CCF on 7 October 2013, and sent to:

Dr Sonja Tesanovic
NIHR Central Commissioning Facility
Grange House
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Twickenham
TW1 3NL