Proposal for Invasive Lobular Breast Cancer (ILC) Research Project

by the Manchester Breast Centre (MBC).

In response to the call by the majority of MPs for a moon shot approach to Lobular Breast Cancer research funding, we are seeking a fast injection of funding - £20m over 5-years – from the Medical Research Council (MRC) to start this vital project as soon as possible. ILC was first discovered 80 years ago and still has no specific treatment. The 22 women diagnosed with this disease in the UK every day have been forgotten.

Based on our meeting on 31st May last year with attendees including MRC - Charlotte Durkin & Isobelle Atkin, LMSP - Susan Michaelis and Tristan Loraine and Manchester Breast Centre – Professor Rob Clarke, we understand the DSIT/UKRI can give extra funding or dedicated funding for a theme such as international partnerships and priority funding i.e. genomics. The Lobular Moon Shot Project fits into this latter priority funding category. ILC is an unmet clinical need.

The research team will be led by Professor Rob Clarke, Professor of Breast Biology at the University of Manchester, with collaboration at its heart, working in partnership with national research organisations such as the Breast Cancer Now Research Centre at the Institute of Cancer Research (ICR) and King's College London (KCL), and the European Lobular Breast Cancer Consortium (ELBCC), of which MBC is a member. Rob has led discussions with AstraZeneca, a UK-based global leader in bringing new drugs into breast cancer, who have agreed to be a commercial partner. The partnership will bring together world-class researchers, scientists, industry and ILC advocates, all with a specific interest in lobular breast cancer, who wish to move forward ILC research at a much greater pace to improve patient outcomes.

Manchester Breast Centre Lobular Breast Cancer Research Project Framework:

The aim will be to more rapidly advance research into ILC, which is a unique type of breast cancer that's long been neglected. ILC has been recognisable as distinct by pathologists for over 80 years. However, recent genomic advances have established its genetic foundation, which is mutation or loss of the ECadherin gene. This genetic change accounts for 15% of breast cancers, affecting 7,500 women in the UK each year, making it the largest segment of breast cancer with no specific, effective treatment.

The research project will address three problems specific to ILC:

1. ILC has a long dormancy period, it often recurs after 10-20 years. The research will look at why it lies dormant, what can be done to kill those dormant cells or to prevent them re-emerging as a cancer.
2. ILC spreads to areas of the body that are different from other breast cancers. Ductal Breast Cancer often spreads to the bones, liver, lung and brain but ILC often spreads to the abdomen, ovaries or the skin. We need to learn why it interacts with those different tissues of the body and how it can be treated once it affects these tissues.
3. There is no specific, effective treatment for ILC, which has lost the ECadherin gene. Other breast cancer types such as HER2 gene-amplified (15%) or those expressing estrogen receptor (ER) protein (75%) have specific, effective such as Herceptin and endocrine therapies, respectively. These have substantially changed outcomes over the last 30 years. For example, 20 years ago, HER2 breast cancers were the most difficult to treat with the worst outcomes, but now HER2+ patients have very good long term survival due to specific, effective treatments such as Herceptin. The aim is to do the same for ILC.

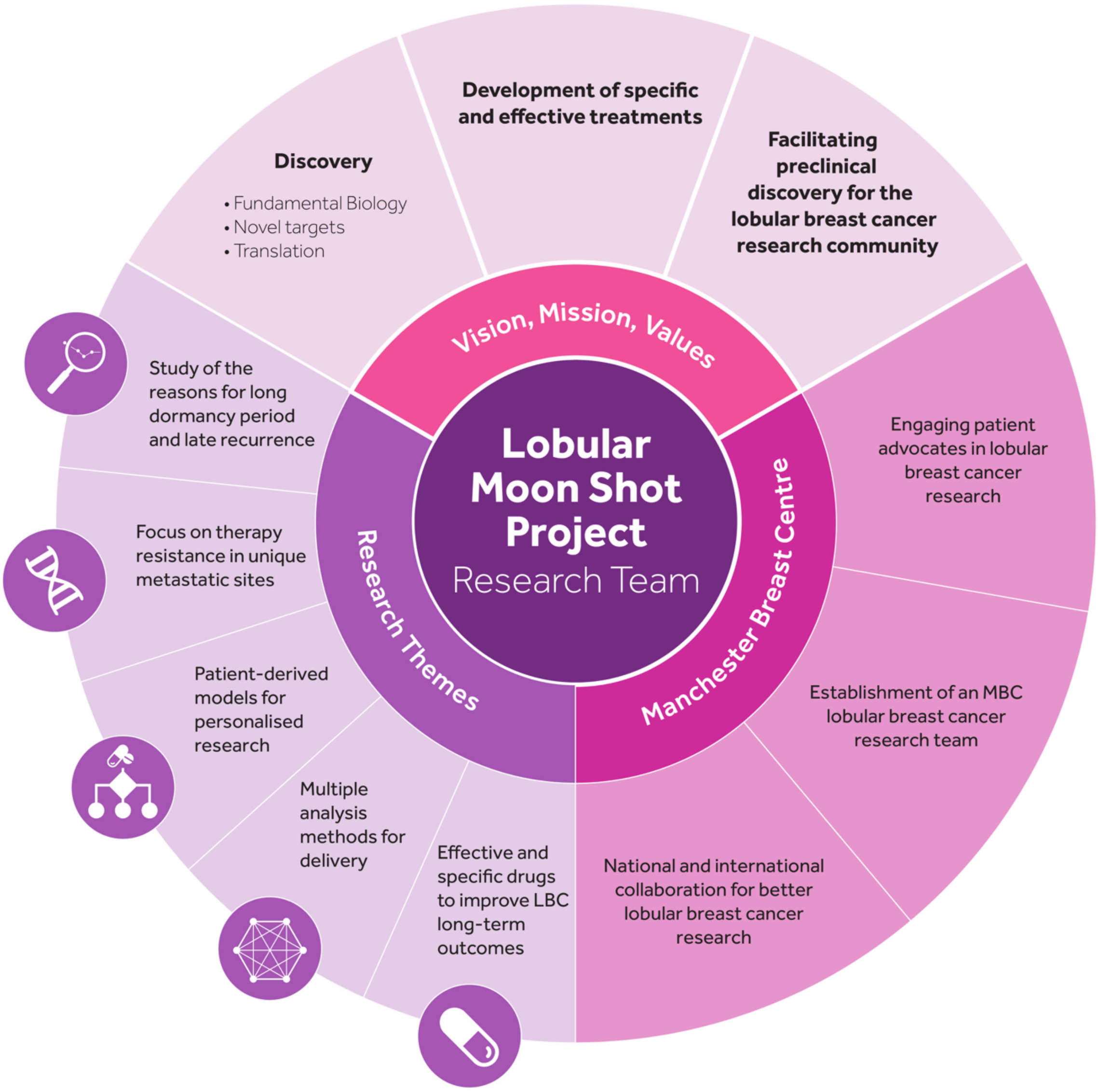
By studying the dormancy, the different patterns of spread to tissues in the body and why it grows there, the team led by MBC can work towards finding a specific, effective therapy for ILC.

The research themes of the Lobular Moon Shot Project will be to focus on resistance to current treatments in the unique tissues that ILC spreads to, to develop and utilise ILC patient-derived models for personalised research, and to implement multiple analysis methods for delivery of specific, effective drugs to improve long term outcomes in ILC (see Figure 1 overleaf). To deliver on the project, MBC have assembled an international team of 24 expert scientists to collaboratively deliver this research. The team will be coming to Manchester on 30th June 2025 to discuss and plan this collaborative initiative in the Manchester Think Tank meeting, the largest of its kind to focus uniquely on the ILC subtype (see page 4), with a round table discussion to be led by Andy Burnham, Mayor of Greater Manchester.

In summary, with effective, targeted funding, the Lobular Moon Shot Project will be ready to tackle this under-researched disease and change the course of patients' outcomes in the future with discovery, preclinical validation and delivery of a specific, effective therapy ready to be trialled in ILC.

LOBULAR
MOON SHOT PROJECT
RAISING FUNDING FOR RESEARCH INTO
LOBULAR BREAST CANCER

Figure 1 Infographic showing how MBC will tackle ILC through addressing the research themes set out below in collaboration with national and international collaborators



Manchester Breast Centre Think Tank Meeting
in collaboration with the European Lobular Breast Cancer Consortium (ELBCC)

Date: 30th June 2025
University of Manchester, UK.

Special Guest:

Andy Burnham (Mayor of Greater Manchester)

Patient Representatives:

Susan Michaelis, Kirsten Spencer, Tristan Loraine, Clare Turner

Scientists:

Manchester Breast Centre: Professors Rob Clarke, Sue Astley and Cliona Kirwan, and Drs Sankari Nagarajan, Bruno Simoes, Hannah Harrison, Frances Turrell and Sue Pritchard.

Institute of Cancer Research (ICR), London: Professors Clare Isacke, Chris Lord and Cathrin Brisken, and Dr Rachel Natrajan.

King's College London (KCL): Dr Eli Sawyer

University College Dublin (UCD): Professor Darran O'Connor

Curie Institute, Paris: Professor Anne Vincent-Salomon

Netherlands Cancer Institute (NKI), Amsterdam: Professors Jos Jonkers and Maleen Kok.

EPFL, Lausanne, Switzerland: Dr George Sflomos

University of Oslo, Norway: Professor Therese Sorlie.

Apologies:

ELBCC: Professor Christine Desmedt (KU Leuven, Belgium)

University of Edinburgh: Professor Val Brunton

University of Pittsburgh, USA: Professors Steffi Oesterreich and Adrian Lee

Huntsman Institute, Utah, USA: Professor Alana Welm

Evidence:

Lobular breast cancer is an unresolved clinical need and should be a priority focus for research beginning as soon as possible.

Journal of the National Cancer Institute:
Invasive Lobular Carcinoma of the Breast: Toward Tailoring Therapy?
https://academic.oup.com/jnci/article/114/11/1434/6758319

National Library of Medicine:
Unique Molecular Alteration of Lobular Breast Cancer: Association with Pathological Classification, Tumor Biology and Behavior, and Clinical Management
https://pmc.ncbi.nlm.nih.gov/articles/PMC11816017/

ResearchGate:
Abstract ED02-01: Biological peculiarities of ILC
https://www.researchgate.net/publication/380301110_Abstract_ED02-01_Biological_peculiarities_of_ILC

ScienceDirect:
E-Cadherin Mutational Landscape and Outcomes in Breast Invasive Lobular Carcinoma
https://www.sciencedirect.com/science/article/pii/S0893395224001509

MDPI:
Deciphering the Clinical Behaviour of Invasive Lobular Carcinoma of the Breast Defines an Aggressive Subtype
https://www.mdpi.com/2072-6694/16/10/1893