# Developing new treatments for invasive lobular breast cancer

## The Lobular Moon Shot Project

## A proposal by The Institute of Cancer Research, London

April 2023

## Introduction

The Institute of Cancer Research, London (ICR) has discovered more new cancer drugs than any other academic institution globally, and led the science that has underpinned many more cancer treatments.

The ICR also has a strong track record of researching cancers of unmet need, and one area of breast cancer research that urgently needs attention is invasive lobular breast cancer (ILC). At present, women with ILC are treated in much the same way as those with other, very different, types of breast cancer. The result of this is that treatment works well for some but not for all. To change this, new and more effective options for ILC are needed.

Thank you for your interest in working with the ICR to address this issue. We understand how passionate you are about making a difference to ILC patients' lives and would like to present the opportunity to improve treatments for these patients through the recruitment of a new postdoctoral fellow, who will be essential in driving forward our work to improve outcomes for ILC. This will be the first step in a larger project to develop more targeted approaches to ILC, and we would be delighted to partner with you in making this vision a reality.

## The Institute of Cancer Research, London

*The ICR's Centre for Cancer Drug Discovery in Sutton*

The ICR is one of the world's leading cancer research organisations. Our mission is to make the discoveries that defeat cancer – and we aim to transform the lives of cancer patients and their families through world-class research.

Our Centre for Drug Discovery houses the largest and most successful academic drug discovery unit in the world. Since 2005, it has discovered 21 drug candidates and taken 12 drugs into clinical trial. A drug called abiraterone, which was discovered and developed by the ICR, was the first treatment shown to be effective in men with advanced prostate cancer.

The ICR is a world-leading higher education institution, a member institute of the University of London, and a charity. Together with our hospital partner, The Royal Marsden, we are rated as one of the top centres for cancer research and treatment in the world.

## How our pioneering research is changing lives

Breast cancer is the most common cancer in the UK, with around 55,200 new cases diagnosed every year. One in seven women will be diagnosed with breast cancer in their lifetime. Survival rates have improved greatly, thanks to a better understanding of the disease and more effective treatments, but there is still much to do.

Scientists in our Division of Breast Cancer Research have been involved in some of the most famous discoveries in the history of breast cancer research. One of our greatest achievements, and one of the most significant discoveries ever made in cancer genetics, was the discovery of BRCA2.

Understanding how the gene is implicated in the development of breast cancer has led to therapies which target cancers associated with BRCA2 and genetic tests that calculate cancer risk.

Our researchers have led studies that have enabled us to discover and develop new breast cancer drugs. For example, we played a leading role in the clinical development of a class of hormonal drugs called aromatase inhibitors, which are now a mainstay of breast cancer treatment in post-menopausal women.

Our research has also underpinned the development of PARP inhibitors, including olaparib, now used in the treatment of BRCA-positive ovarian cancer and showing promising results in trials in breast cancer.

We have recently shown in clinical trials the effectiveness of two drugs – the chemotherapy carboplatin, which we discovered, for the treatment of triple-negative breast cancer, and palbociclib, a targeted drug for advanced breast cancer, which we developed. The latter marks one of the biggest advances in treatment for women with advanced breast cancer in the last two decades. More than 90,000 patients have already been prescribed palbociclib.

**'I'm on the 52nd cycle of palbociclib and my cancer is currently stable. I take my pill every morning, and I get on with my life. Palbociclib allows me to live a good life with cancer – and I want all cancer patients to have this hope and optimism for the future.'**

**Christine O'Connell** was diagnosed with secondary breast cancer in February 2018.

## Our approach to improving outcomes for ILC patients

**'Many people often think of lobular breast cancer as a 'forgotten' type of breast cancer. What we want to do is come up with new ways of treating it, by identifying smarter, kinder treatments.'**

**Professor Chris Lord**
Deputy Director of the Division of Breast Cancer Research.

While we are delighted with the progress we have made so far in breast cancer research, 11,000 people are still losing their lives to breast cancer each year. ILC represents 15 per cent of all breast cancers diagnosed. Unlike ductal breast cancer, they grow in a line or as single cells and rarely form a lump. This can make diagnosing ILC more challenging and lead to later stage diagnoses, which makes the cancer harder to treat successfully.

Although it comprises a significant fraction of the breast cancer population and the molecular composition of ILC is partially understood, targeted approaches to ILC treatment do not yet exist.

One approach to finding new treatments is to identify weaknesses in ILC cancer cells that do not exist in normal, healthy cells. The work we propose is aimed at doing just this: identifying ways of killing ILC cancer cells, whilst leaving normal cells unharmed. The intention in doing this is that new treatments targeting these weaknesses will be very effective in clearing cancer cells from the body without causing so many of the side effects associated with existing treatments, such as traditional chemotherapy.

To achieve this, we will exploit one key feature of cancer cells in ILC patients. ILC cancer cells, when compared to normal cells, lack a protein called E-cadherin. While not having E-cadherin allows ILC cancer cells to behave in an abnormal way, it also makes each cancer cell rely on other proteins that are not needed in normal cells. If we can identify the proteins that ILC cancer cells without E-cadherin rely on, and then stop these working, we should be able to kill ILC cancer cells but not normal cells.

We have already identified a series of different proteins that ILC cancer cells without E-cadherin rely on. What we need to do now is three things:

- Work out which of these proteins is the best one to inhibit so that we kill cancer cells and leave normal cells unharmed. If we can do this, we can design new drugs that hit this particular protein.
- We also need to understand whether drugs already used to treat other types of cancer can inhibit these proteins. If we can work this out, we can start drug trials much sooner to see if these existing drugs could be used to treat ILC.
- We need to see if inhibiting these proteins works well when we do this at the same time as using drugs already used in breast cancer treatment. This is important as drugs used in cancer treatment are often used together (combination therapy) to make these more effective.

We believe that if we can address these three questions over the next five years, we will make important steps forward in improving the way people with ILC are treated.

## Our ambitions

Answering these questions will be a key first phase towards a better understanding of the biology of lobular breast cancer, how we can identify new drug targets for this disease and to the point where they can be assessed in patients through clinical trials.

We believe that:

- For £500,000, we could recruit a postdoctoral fellow to drive forward our work to create more and better treatments for patients with ILC.
- For £2m, we could significantly scale up our efforts by recruiting four postdoctoral fellows who can advance our work to understand how lobular breast cancers spread beyond the breast.
- For £5m, we could set up a new pipeline for identifying new drugs to use in ILC.
- For £10m, we could set up the first of a series of new clinical trials testing new treatments in women with ILC.
- For £20m, we could set up a second clinical trial testing new treatments in women with ILC.

Each amount will build on the one before in terms of what we can achieve.

## Funding a new leader in ILC

Our first step in realising our ambitions is to focus on addressing the knowledge gap described in the points above, for which the recruitment of a postdoctoral fellow is essential. This individual, who is already trained to PhD level, will drive forward our work to create more and better treatments for patients with ILC.

The five-year budget for this post, including on-costs and consumables are as follows:

| Postdoctoral Fellow | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | TOTAL |
|---|---|---|---|---|---|---|
| | | | | | | |
| Salary (including on-costs) | £62,209 | £64,075 | £65,998 | £67,978 | £70,017 | £330,277 |
| Consumables | £19,000 | £19,000 | £19,000 | £19,000 | £19,000 | £95,000 |
| PI (10%) | £17,518 | £18,044 | £18,585 | £19,143 | £19,717 | £93,007 |
| Essential laboratory costs | £3,110 | £3,204 | £3,300 | £3,399 | £3,501 | £16,514 |
| TOTAL | £101,837 | £104,323 | £106,883 | £109,520 | £112,235 | **£534,798** |

## Next steps

We would be delighted to work with you to engage with any interested parties who could consider a significant contribution towards recruiting this new post. Thank you for all your efforts towards supporting the ICR towards developing new and better treatments for ILC patients.

To donate to this work, please visit the Lobular Moon Shot Project website for details of how to make an instant direct donation or to obtain bank transfer details in GBP, USD or Euros to the ICR.

## Notes

This document and project were drawn up by the ICR at the request of Dr Susan Michaelis for the Lobular Moon Shot Project.

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