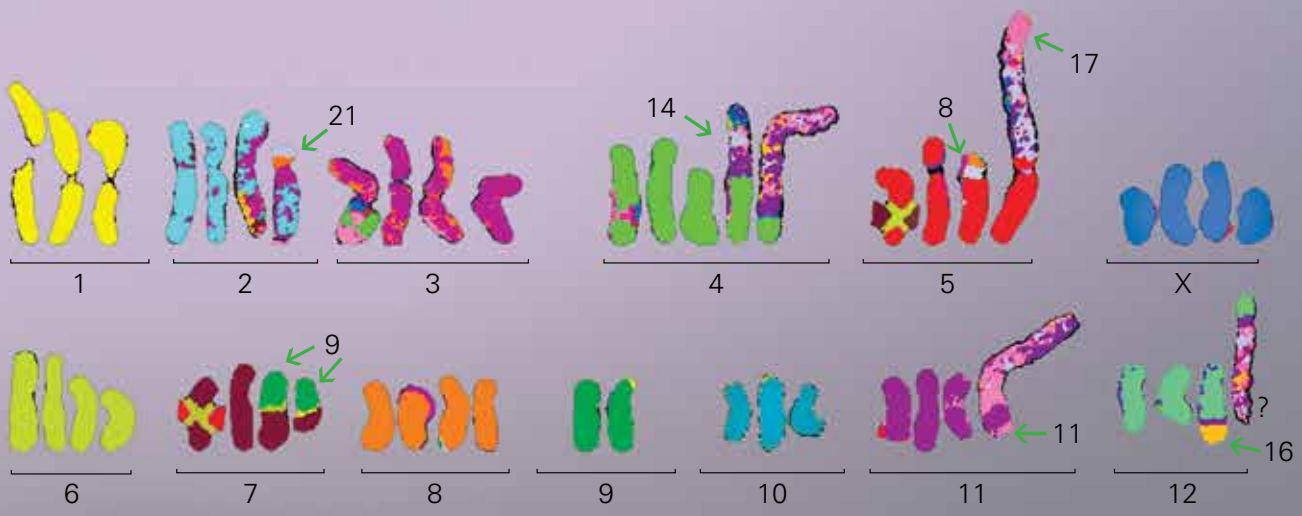


Genomic Cancer Medicine Program

GARVAN INSTITUTE OF MEDICAL RESEARCH

Genomic cancer medicine is the future of all cancer treatment and its greatest impact will be in rare, high-mortality cancers.

It uses the latest genome sequencing approaches to select treatments based on the genetics of the cancer, rather than where it is growing in the body, for example, breast, colon or skin. This makes it possible to personalise cancer treatment, giving the right drug to the right patient at the right time. Genomic information also makes it possible to understand genetic cancer risk better than ever before, and to detect cancers earlier.

The Genomic Cancer Medicine Program is an innovative suite of clinical trials that matches therapies, prevention and screening methods with individuals on the basis of genetic information. It gives hope to patients who have exhausted other treatment options and the outcomes will help us better treat and prevent rare and less common cancers, and all cancers, in years to come.

THE STATISTICS

186 types of rare and less common cancer

In 2017 **52,000** Australians will be diagnosed with one of these cancers

25,000 will die

This accounts for **30%** of cancer diagnoses and **50%** of cancer death in Australia.

RARE CANCERS INCLUDE:

brain
soft tissue sarcoma **haematological**
oesophagus **gallbladder**
bladder **ovary** **oropharynx**
stomach **pancreas** **chordoma**
acute myeloid leukaemia

FUNDING $

Research into rare cancers attracts only 2% of research funding

A patient diagnosed today with a rare or less common cancer is almost **twice as likely to die** as a patient with a common cancer.

FROM GENETICS TO GENOMIC MEDICINE

The **genome** is the complete set of genetic information we inherit from our parents. A **gene** is a section of DNA that is transferred from a parent to a child and determines some characteristic of that child, such as eye colour or height.

DNA is a molecule that is made up of four basic building blocks represented by the letters A, C, G and T. The sequence of these letters forms the instructions in the genome. Sections of these DNA letters, 'read' together, make up genes. A human genome contains around 6 billion of these DNA letters.

Molecular screening is another term for genomic testing.

GARVAN'S GENOMIC CANCER MEDICINE PROGRAM

The Genomic Cancer Medicine Program is an innovative suite of clinical trials and studies that matches therapies with individuals on the basis of genomic information.

Developed by the Garvan Institute of Medical Research, the Genomic Cancer Medicine Program represents a new approach to personalising cancer treatment, screening and prevention. The program has two main focuses:

Molecular Screening and Therapeutics Clinical Trial (MoST) – a clinical trials program that matches patients to therapies (more on page 6);

Genetic Cancer Risk in the Young Study – a risk management program for families with high genetic cancer risk (more on page 8).

The Genomic Cancer Medicine Program has a major focus on rare and less common cancers, which have previously been neglected in cancer research.

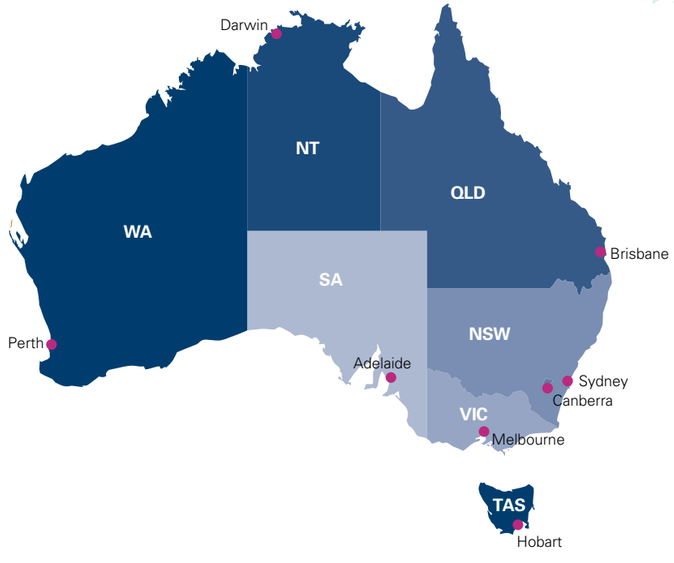
GENOMIC AND PERSONALISED MEDICINE FOR ALL AUSTRALIANS

The Genomic Cancer Medicine Program is a national program, and it is critical that all Australians diagnosed with rare and less common cancers can access its services. The need of patients with rare and less common cancers is so great that Garvan, along with our partners, is committed to seeing the Genomic Cancer Medicine Program rolled out across Australia.

We are in negotiations with several research centres, and are looking to partner with organisations in every state and territory to provide all Australians with access to the Genomic Cancer Medicine Program.

Currently, there are 400 patients enrolled in the Genomic Cancer Medicine Program (August, 2017). Yet, 52,000 people are diagnosed with rare and less common cancer each year in Australia alone.

> "It's my belief that research funding correlates directly with survival rates. The more research, the better the outcomes for patients."
>
> **– Professor David Thomas**



PARTNER INSTITUTES

GARVAN INSTITUTE OF MEDICAL RESEARCH, SYDNEY

The Garvan Institute is one of Australia's leading medical research institutes. It's researchers pioneer studies into some of the most widespread diseases affecting the community today.

The Institute's focus is on understanding the role of molecular and cellular processes in health and disease as the basis for developing future preventions, treatments and cures.

ST VINCENT'S HOSPITAL, SYDNEY

St Vincent's Hospital is one of Australia's most iconic hospitals, which functions as a full service acute public teaching hospital.

Part of the NSW-based arm of St Vincent's Health Australia, the Hospital provides significant training and research activities, housing several specialty units that are internationally recognised as centres of excellence.

NHMRC CLINICAL TRIALS CENTRE, SYDNEY

The NHMRC Clinical Trials Centre runs large multicentre investigator-initiated clinical trials, works with Australasian and international collaborative research groups, integrates evidence, develops new clinical research methods and offers clinical research educational programs.

The Clinical Trials Centre's aim is to translate research evidence into improving health outcomes.

MEET THE TEAM

PROFESSOR DAVID THOMAS

Head of Garvan's Cancer Division and Genomic Cancer Medicine Laboratory, Director of The Kinghorn Cancer Centre

DR MANDY BALLINGER

Leader of Garvan's Genetic Cancer Risk Group

DR ANTHONY JOSHUA

Director of Oncology, The Kinghorn Cancer Centre

PROFESSOR JOHN SIMES

Director of the NHMRC Clinical Trials Centre

MOLECULAR SCREENING AND THERAPEUTICS CLINICAL TRIAL

The Molecular Screening and Therapeutics (MoST) clinical trial is the product of a close collaboration between Garvan and the NHMRC Clinical Trials Centre. It personalises experimental treatment based on an individual's unique personal and cancer genetic profile.

Professor David Thomas says, "There are new medicines with applications across a range of cancers, many of which are sufficiently uncommon that there is neither the patient population nor the commercial opportunity for extensive traditional clinical trials to be conducted or funded. This has led to the emergence of 'basket trials' where, rather than focusing on a tumour's anatomical location, such as the ovaries, patients say with ovarian cancer, pancreatic cancer, sarcoma and other cancers, but who have a shared harmful genetic variant, are treated with a drug that may target the variant."

Until recently, clinical trials were generally used to test one new treatment, with some patients getting the new drug and the others getting an existing drug or placebo. The MoST protocol tests multiple treatments at the same time and, importantly, all participating patients in the MoST trial receive a treatment. The advent of genomic medicine means that treatment is guided by the genetic make-up of the patient and their illness.

First, all patients, and their tumours where possible, are genomically screened to see if they are suitable for a trial and if there are variants that can guide the treatments that can be trialled. These 'signal-seeking' trials are looking to see if a treatment will work, or work more effectively than another treatment. Not everyone will have indicators for the drugs that are being trialled and these patients will be treated with immunotherapies (drugs that stimulate the anti-tumour immune response, enabling immune cells to attack cancer cells) or referred to other clinical trials. Professor Thomas and his team are looking to understand how targeted therapies work and to find new biomarkers that can predict which patients will benefit from these treatments.

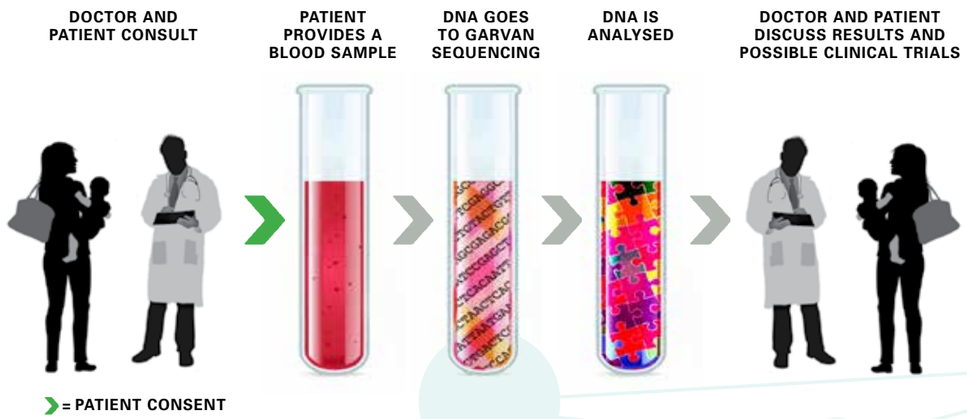
After screening, patients are offered either:

1. Participation in the MoST clinical trial where a targeted therapy is matched to the molecular signature of the individuals cancer;
2. Where a clear molecular target or signature is not identified, participants may be offered the latest in cancer immunotherapies as part of MoST; or
3. Recommendations to other clinical trials as appropriate.

All participants are informed of the results of the screening of their tumour tissue through their own doctors.

> "All participating patients in a MoST trial receive a treatment."

GENOMIC CANCER MEDICINE PROGRAM



> "In early 2017, I was enrolled into the MoST immunotherapy clinical trials program at Garvan...I have grown stronger and more determined to take each day as it comes and beat this cancer."

PATIENT STORY: DARIN MALLAWARACHCHI

In 2012, doting grandad, Darin Mallawarachchi, age 59, was at home carrying his grandson when he slipped on the staircase and hit his tailbone. The ensuing scan revealed a 3cm chordoma tumour, a rare type of bone cancer, on the sacrum, the triangular bone just above the bottom tip of the spine.

Darin had been in good health, going to the gym and very active. "Although I was lucky that the tumour was detected very early, it was still such a shock," says Darin. "We are a very close family – I have three grown-up daughters, and three grandchildren, with another one on the way this year. My whole family is very worried, and stressed."

Following successful surgery to remove the tumour in September 2012, it took Darin six long months to recover from postoperative complications. On MRI scan in December 2013, a new 2cm tumour of was detected. This was treated with stereotactic radiation in March 2014, but unfortunately the tumour continued to grow. As a result, in March 2015, Darin underwent radio frequency ablation treatment, instead of surgery, to remove the tumour as far as possible. As the tumour was almost touching a nerve, saving the nerve meant not eradicating the whole tumour.

"Follow-up scans, in October 2016, showed the residual tumour had increased in size, and in November 2016, I was treated with radio and microwave ablation therapy.

"I would like to thank the doctors and surgeons who provided me with an excellent standard of care.

"Now I have pains and aches at the base of my spine and right leg, which is also now weaker. Following all the procedures that I underwent, I also have bladder and bowel problems.

"In early 2017, I was enrolled into the MoST immunotherapy clinical trials program at Garvan, following introduction by Rare Cancers Australia. Hopefully the immunotherapy treatment can destroy the residual cancer cells, which are at the base of the nerve.

"It is true that life is different now and I am not quite the same person as before, however, life continues to hold much happiness, and hope. I am able to keep positive. I have grown stronger and more determined to take each day as it comes and beat this cancer.

"Garvan is providing pioneering research and clinical trials treatment to cancer patients in Australia, but the availability of the clinical trials isn't widely known. It's vital that more patients have access to rare cancer drug trial programs.

"I am excited knowing that Garvan has made remarkable strides toward new treatments that will mean better outcomes for everyone affected by this rare disease. I hope that supporting and being part of Garvan's research will help in finding a drug or medical solution in the future for those who are diagnosed with rare cancers."

GENETIC CANCER RISK IN THE YOUNG STUDY

Perhaps the greatest opportunity to reduce death rates from cancer lies in more effective early detection, to allow curative treatment. For this, it is critical to understand the genetic basis for risk, especially amongst those who develop cancer at an early age. The Genomic Cancer Medicine Program's Genetic Cancer Risk in the Young study is shedding new light on how we understand cancer risk.

In the past we have only understood cancer risk at the level of the single gene, like BRCA1 or BRCA2 for breast and ovarian cancer. We now know that there is actually a complex interplay of numerous different genetic factors that together affect cancer risk.

Carrying several of these genetic variants markedly increases an individual's cancer risk, so that the cancer tends to occur earlier. Researchers in the Genetic Cancer Risk in the Young study are working with people who have developed cancer at an early age, so as to learn more about the precise genetic factors that impact on cancer risk.

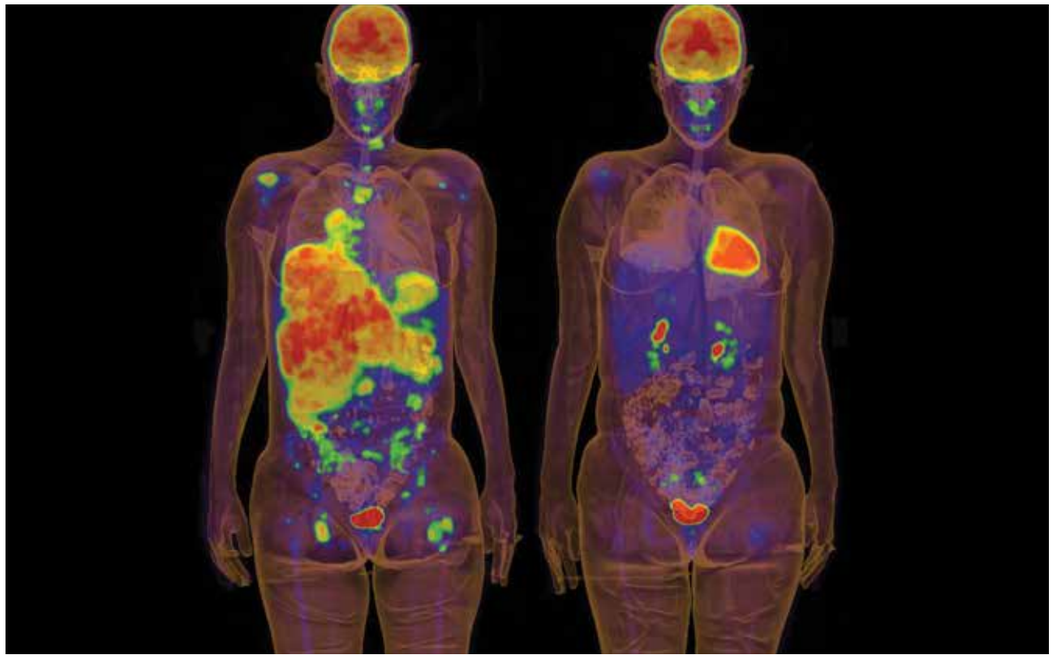
Dr Mandy Ballinger explains: "Knowing the genetic drivers that give a person an increased risk of cancer allows us to more precisely match individuals with the best possible treatment and monitoring measures.

"As part of this world-first research, we are following up people identified as being at increased cancer risk in the Genetic Cancer Risk in the Young study who will be offered tailored cancer surveillance and risk management as part of the Surveillance in the Multi-Organ Cancer prone syndromes (SMOC+) study. Already in SMOC+, from 30 at-risk individuals screened, four were found to have asymptomatic, high-grade cancers that were treated with curative intent."

Cancers found early include an osteosarcoma at age 24, two early onset prostate cancers in men in their mid-forties, as well as an asymptomatic sarcoma in a 53-year-old woman. Researchers have already identified a number of new genetic variants that indicate cancer risk.

"We have only scratched the surface of cancer's genetic underpinnings," says Dr Ballinger.

"Ultimately, we want to identify the entire set of genetic mutations that affect the risk of developing cancer."



PATIENT STORY: ZARA D'COTTA

Zara D'Cotta was diagnosed with breast cancer nine days before her 30th birthday – and then two years later, she was diagnosed with a melanoma on the morning of her breast cancer anniversary.

"I'd been for a walk along the St Kilda foreshore at sunrise to commemorate it and reflect on how far I had come," says Zara. "It finally all seemed like a distant memory, but life can change so quickly.

"I spent my second birthday in three years recovering from surgery, waiting to find out if my cancer had spread."

Zara had a lumpectomy for her localised breast cancer, but then went on to have six weeks of daily radiotherapy to minimise the risk of recurrence. "It felt completely bizarre as a fit, healthy young woman, to leave my corporate job every day to sit in a white hospital gown, surrounded by people much older than me, waiting to be zapped by a machine so big it looked like it belonged on a space ship. While there were no visible signs of the side effects it was physically exhausting and mentally challenging."

Zara then started the anti-hormone medication, tamoxifen. "My side effects were so severe I had to stop working. Just putting one foot in front of the other felt like a huge task. At its worst I felt hazy and couldn't do basic things like drive my car. I'd burst into tears for no real reason. After 15 months, I stopped taking tamoxifen because of the degree to which it was affecting my quality of life. Thankfully, my melanoma also hadn't spread to any nerve or blood cells. I had surgery to remove all the surrounding tissue and didn't require any further treatment.

"It was an extremely difficult time for us all. I don't think I'll truly appreciate or understand what it must have been like for my mother until I have children myself, but I know that as a parent you want to do whatever you can to protect your child. To be in a situation like that and not be able to do anything, and also have to stay strong for your child, must have been awful and terrifying. It was when I received the call from my surgeon to say that my breast cancer hadn't spread and my mum burst into tears with relief that I realised how worried she had been.

"My mum was diagnosed with breast cancer one month after my breast cancer diagnosis. It was a different type of cancer to mine, and I tested negative for the BRCA gene mutation, so we are not sure whether they are genetically linked.

"I consider myself very lucky to be cancer free, but the cancer treatments and stress from the two cancer diagnoses have taken their toll. I have learned so much because of this experience though and the knowledge I have gained, and continue to gain on this journey is hugely empowering.

"I am really excited to be part of the Genetic Cancer Risk in the Young study. When I was first diagnosed with cancer four years ago, I was prepared to accept that I may never know why I got cancer. To think that I may soon know the reasons is absolutely mind-boggling. I am in awe of the work of the wonderful team of researchers at Garvan – the discoveries they have made fill me with great hope that we will see a cure for cancer in my lifetime."

WE NEED YOUR SUPPORT

We are delighted to update you on the difference that the Genomic Cancer Medicine Program is making in the lives of those with rare cancers and their families.

The Genomic Cancer Medicine Program is helping rare cancer patients to have better outcomes.

Rare cancers account for 50% of cancer deaths, yet attract only 2% of cancer funding.

Every life is valuable and all people with cancer have the same right to life. But while mortality rates for common cancers have dropped, rare cancer rates – and deaths – are actually rising.

We have been fortunate to receive investment from the NSW Government and generous individuals and organisations to allow Garvan to establish the Genomic Cancer Medicine Program. However, additional funding is vital to make the Program nationally available for the benefit of all Australians impacted by rare and less common cancers.

We urgently need your help to support the Genomic Cancer Medicine Program. It costs us $16,000 per patient for the MoST clinical trial and $1500 per patient per year for the screening phase of the Genetic Cancer Risk in the Young study. Please, if you can, consider supporting this innovative program for people with rare cancer.

Mr Andrew Giles
Chief Executive Officer
Garvan Research Foundation

If you would like to discuss supporting the Genomic Cancer Medicine Program, please contact:
Ms Mara-Jean Tilley
Head of Philanthropy
Garvan Research Foundation

Phone: +61 (0) 2 9295 8513
Email: m.tilley@garvan.org.au

HOW YOU CAN HELP

We require significant philanthropic investment to bring new treatment, screening and prevention options to those with rare cancer.

MOLECULAR SCREENING AND THERAPEUTICS CLINICAL TRIAL REQUIRES:

$256,000 per module

$16,000 per patient

Each module includes **16** patients.

GENETIC CANCER RISK IN THE YOUNG STUDY REQUIRES:

$3500 per patient to be enrolled on to the study. This includes blood and data collection, genome sequencing and analysis.

Approximately **10%** of patients enrolled will go on to surveillance.

$1500 per year per patient on surveillance (whole body MRI).

As at August 2017, there are 400 patients enrolled in the Genomic Cancer Medicine Program. Yet, 52,000 people are diagnosed with rare and less common cancers each year in Australia alone.

A LASTING LEGACY

There are many opportunities to support Garvan's Genomic Cancer Medicine Program.

Your investment will support intellectual capabilities, clinical trial infrastructure and make a difference in people's lives.

Wendy, Cathie and Paul.

FAMILY STORY: PAUL AND WENDY JEANS

Paul and Wendy Jeans' daughter Cathie was a vibrant, fit and busy wife and mother of three teenage boys, just approaching her 49th birthday, when she was diagnosed with gallbladder cancer at the end of 2014.

"Cathie had had occasional abdominal pain and bloating and some gastric reflux, which was thought perhaps to have been gallbladder related, though not sufficiently worrying to her GP to have any tests done," says Paul Jeans.

"Our family has always been very close and Wendy and I have been deeply involved in Cathie and her husband Joe's life, holidaying together, looking after the boys, etc. Cathie's diagnosis of gallbladder cancer and prognosis of only six months was just devastating.

"Cathie was typically stoic and, as her diagnosis was somewhat inconclusive, we optimistically hoped that the tumour might have been a secondary metastasis from a potentially more treatable primary colon cancer."

Indeed, Cathie was initially treated with chemotherapy drugs for colon cancer, but after a number of failed courses and the deterioration of her liver function, in March 2015 Cathie underwent a major operation to install stents and bypass part of her bowel. She also underwent a course of chemotherapy drugs for gallbladder cancer, but this treatment did not produce any improvement either.

"Through my association with University of Newcastle and the Hunter Medical Research Institute, it was suggested that we have Cathie's genome mapped to find chemotherapy drugs that may be effective in her particular case. This analysis confirmed that her current chemotherapy drugs would be unlikely to work, but it also suggested that two other drugs, not normally used with gallbladder cancer, may have potential."

After three cycles of treatment, this third combination of chemotherapy drugs resulted in an 80% reduction in Cathie's cancer markers, but by then it was too late to save Cathie. She died at the end of August 2015.

WE NEED BETTER OUTCOMES

The Genomic Cancer Medicine Program puts people at the centre of research and recognises the exceptional value of every life. In the past it has been thought that rare cancers are simply too hard to cure. People with rare cancer have been left behind with little to no hope of survival. Now, with genomics, we can look at cancers very differently and identify individual triggers for individual cancers, allowing treatments to be tailored for many more people. Cancer is a devastatingly far-reaching disease. Everyone diagnosed with cancer has the right to treatment and a right to live.

> As a family, we are targeted philanthropists, we give to causes about which we are passionate. Remembering Cathie is of the utmost importance to us and we feel we can do that most effectively through supporting Professor Thomas's work at Garvan, and thereby making a real difference to others who may find themselves in her situation.

"Cathie's brave fight had totally exhausted her, and the complexity and seriousness of her situation meant that she spent most of her last six months in hospital, rather than with her family. The impact of not only losing one's child, but seeing her devastated physically and wracked with pain is the most painful experience a parent can have. You continue living, but it is in a world that is very different from the one you enjoyed with your child. Cathie's husband Joe, and three boys miss her enormously and Cathie's sister and brother also continue to be deeply affected."

The Jeans family has learned difficult things about 'rare' and less common cancers.

"We now know that some rare cancers are extremely difficult to diagnose and many GPs are not equipped to do so. We also know that personalised treatment, determined through genetic analysis, is essential and it is possible that drugs designed for one purpose may work in another situation.

"We need to try and determine people who may have a particular predisposition to rare cancers. We have experienced other cancers in our family, but none have been terminal. Our wider group of friends have not all been so fortunate. The public needs to be more aware of rare cancers and their significance to the Australian community.

"The 'soft' side of patient care is also extremely important in situations like Cathie's. Some of her doctors lacked the necessary interpersonal skills and that, in itself, negatively impacted her condition.

"Meeting Professor David Thomas at Garvan convinced us of the value of his ideas. Apart from his particular goals, his approach to the experimental model – large steps rather than incremental change requiring expensive and time-consuming trials – has real potential to change the way we go about medical research.

"As a family, we are targeted philanthropists, we give to causes about which we are passionate. Remembering Cathie is of the utmost importance to us and we feel we can do that most effectively through supporting Professor Thomas's work at Garvan, and thereby making a real difference to others who may find themselves in her situation."

Q&A: GENOMIC CANCER MEDICINE PROGRAM

What is the Genomic Cancer Medicine Program?

Garvan's Genomic Cancer Medicine Program is a major clinical trials initiative that seeks to provide targeted treatment strategies for individuals with advanced rare or less common cancers; to understand the genetic drivers that give an individual a high genetic cancer risk; and to provide risk management approaches to individuals and families at high risk.

Who can access the Program?

The Program has a major focus on those with rare cancer.

How do you enrol in the Program?

If you're interested in learning more about enrolling into the Program, please contact gcmp@garvan.org.au.

What is a rare cancer?

Rare and less common cancers – also known as neglected cancers – are defined as those cancers that affect fewer than 1 in 12,000 people. While rare individually, collectively rare and less common cancers account for 30% of cancer diagnoses and 50% of cancer deaths in Australia.

Common cancers like breast, prostate, colorectal, lung and skin cancers make up the majority of diagnoses in Australia. However, there are 186 types of rare cancer from ovarian cancer to chordoma, a cancer of the spine.

Disproportionately affecting young people, there are fewer treatment options available for patients with these cancers than for those with more common cancers.

What treatments are used in the Molecular Screening and Therapeutics clinical trials?

Therapies include novel drugs, which are matched to specific biomarkers, and immunotherapies.

Why are there higher mortality rates for rare cancers?

There are a number of reasons for the high mortality rates for rare and less common cancers. These include lack of focused multidisciplinary care, incorrect or delayed diagnosis and lack of access to new and emerging treatments.

Why are clinical trials important?

Clinical trials are essential to develop new therapies, and there is ample evidence that clinical trials represent the best, most cost-effective standard of care for cancer patients. However, such trials are rarely available to patients with these cancers.

How was the Genomic Cancer Medicine Program established?

The Genomic Cancer Medicine Program was developed by the Garvan Institute in partnership with the NHMRC Clinical Trials Centre. In 2014, the NSW Government invested in the establishment of the Program as part of the Sydney Genomics Collaborative. It has been enabled by the Garvan Research Foundation thanks to the generous support of its philanthropic benefactors.

However, this Program has only just begun to reveal the extent of the unmet need.

MORE INFORMATION ABOUT THE GENOMIC CANCER MEDICINE PROGRAM

All component studies of the Genomic Cancer Medicine Program have been approved by the St Vincent's Hospital Sydney Human Research Ethics Committee, which operates under the requirements of the NHMRC's National Statement on Ethical Conduct in Human Research (2007), the Australian Code for the Responsible Conduct of Research (2007), and for research specific to NSW, the NSW Supplement to the National Statement (2008).

For patient information please contact gcmp@garvan.org.au.

PARTNERS AND COLLABORATORS

The Genomic Cancer Medicine Program (GCMP) was established as part of a long-term investment by the NSW State Government in using genetic technologies to improve patient outcomes.

GCMP builds on partnerships across multiple academic research organisations and cancer centres, the public health sector, and the pharmaceutical industry. Major partners include the NHMRC Clinical Trials Centre (University of Sydney), St Vincent's Hospital Sydney and pharmaceutical companies Roche, AstraZeneca and Pfizer, Rare Cancers Australia and the Vodafone Foundation Dreamlab project.

NSW GOVERNMENT Health

NHMRC Clinical Trials Centre

ST VINCENT'S HOSPITAL SYDNEY

Roche

AstraZeneca

Pfizer

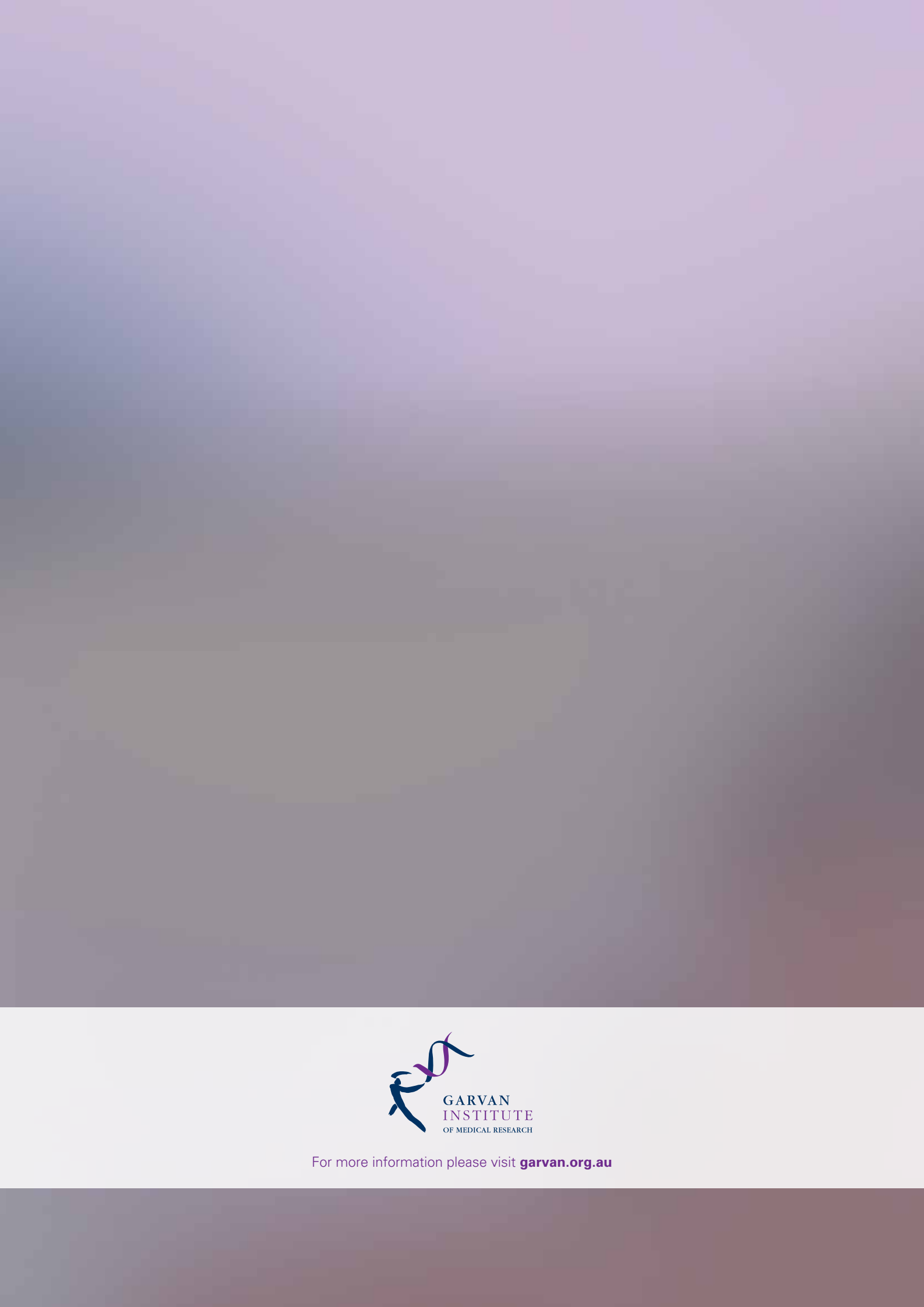
rare cancers AUSTRALIA

Vodafone Foundation

GARVAN RESEARCH FOUNDATION

The Garvan Research Foundation supports the work of the Garvan Institute, tasked with raising and administering vital funds from private individuals, trusts and foundations and corporate and community groups.

Garvan Research Foundation's income has grown from a fundraising base of $110,000 in its first year to more than $30 million in 2016. The remarkable success of the Foundation's activities is having a catalytic impact on the Institute's ability to make scientific contributions that will improve human health.



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For more information please visit **garvan.org.au**