Walter+ Eliza Hall Institute of Medical Research
DISCOVERIES FOR HUMANITY
National Drug Discovery Centre

National Drug Discovery Centre

Monday 9 September 2019

Guillaume Lessene
New Medicines and Advanced Technology - Theme Head

Helene Jousset
Head of the Screening Laboratory

Walter and Eliza Hall Institute of Medical Research

Outline

- National Drug Discovery Centre overview
- Our capabilities
- How you can benefit
- How to apply
- Get in touch

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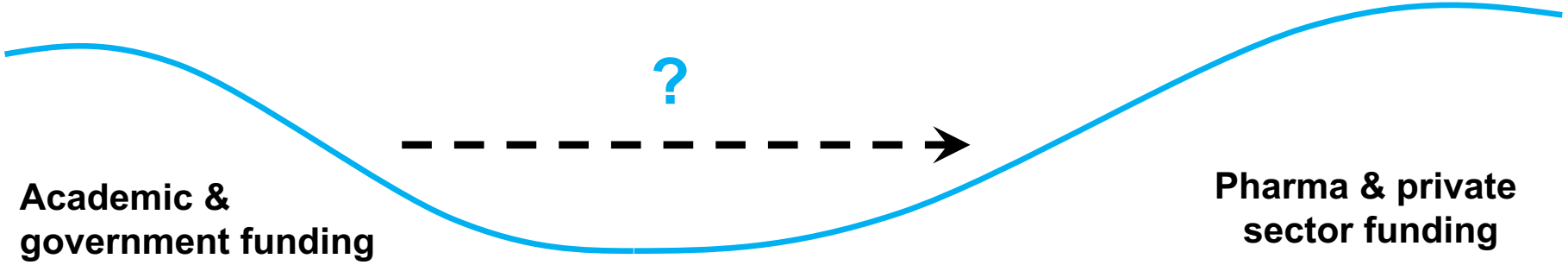
Crossing the valley of death



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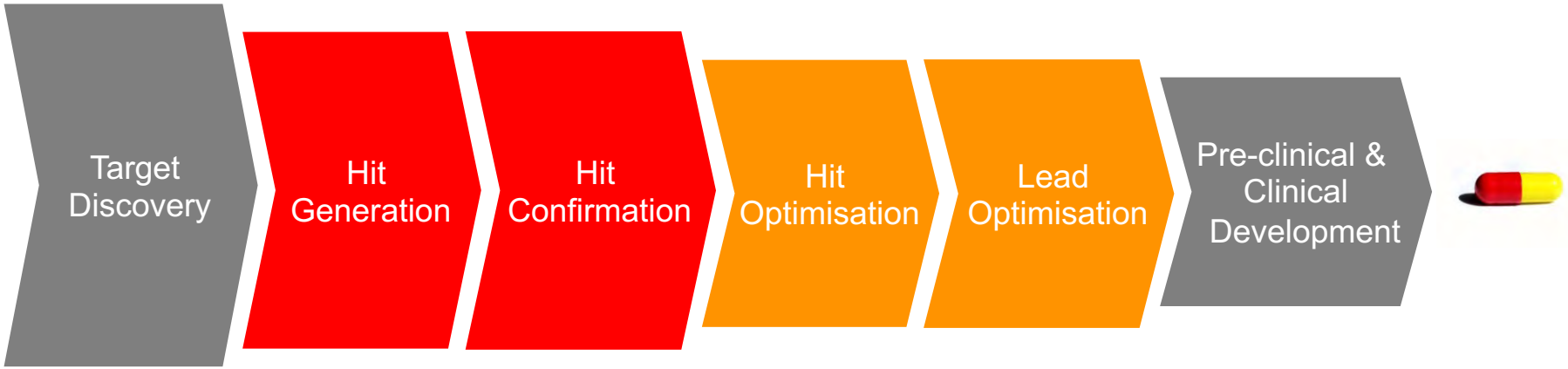
The drug development pipeline

Hit Discovery

Hit-to-Lead



Our drug discovery experience

- Established academic drug discovery infrastructure in 2001:
  - High throughput screening
  - Medicinal chemistry
  - Structural biology
- More than 100 collaborations over the last 10 years
  - Academic, pharma and biotech
- Multiple high throughput screens

Venetoclax development

Apoptosis
Programmed Cell Death

→

ABT-199

1988
Discovery of the role of BCL-2 in cancer (Vaux *et al.*)

2002
Drug discovery initiated at WEHI

2007-2011
Collaboration with Genentech and AbbVie

2011
First human trial at Royal Melbourne Hospital

2016
FDA approval for subset of CLL patients

Background to the NDDC

- Funding proposal to Victorian State and Australian government:
  - To accelerate the translation of new biological discoveries into early stage drug leads to get medicines to patients sooner
  - Create a national hub for high throughput screening
  - Strengthen national collaboration and connectivity between biomedical research institutions

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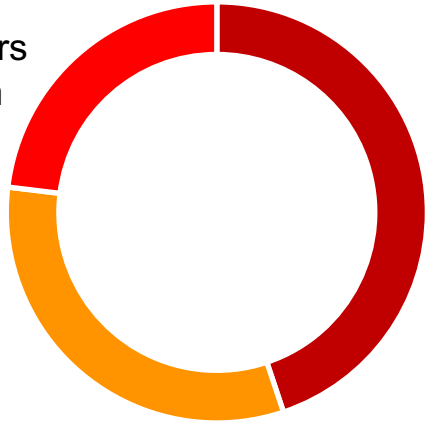
Funding in 2018-2019

Victorian Government
$18M
Instrumentation/additional readers
Compound management system
Protein production



WEHI and philanthropy
$35M
New laboratories and infrastructure

Australian Government
$25M
Over 4 years
Subsidised screens for Australian researchers

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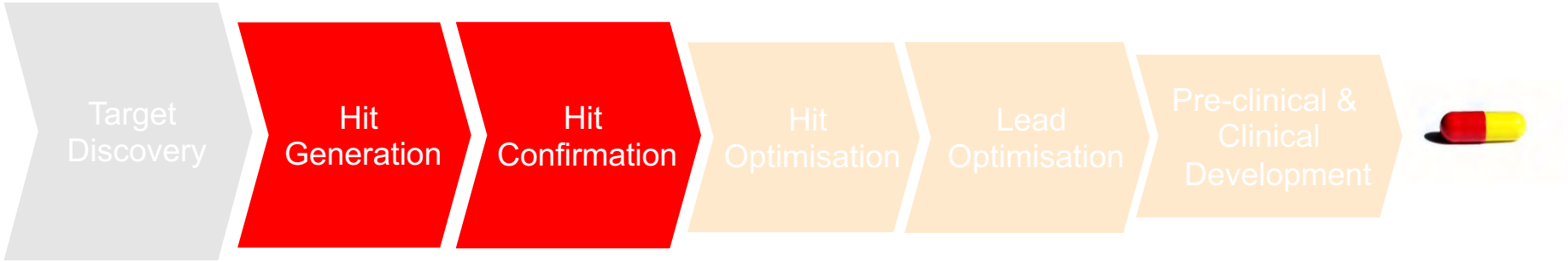
Where the NDDC fits

Hit Discovery

Hit-to-Lead



- NDDC aims to provide support for the hit discovery stage

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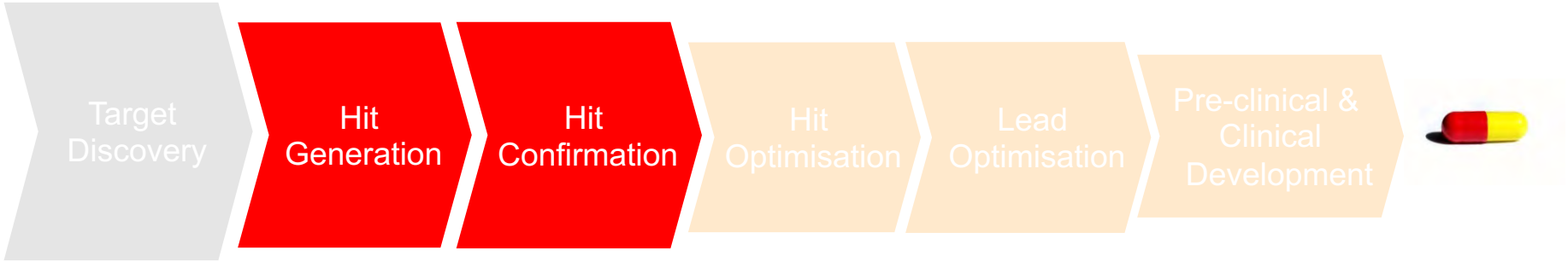
Hit Discovery in more details

Hit Discovery

Hit-to-Lead



Assay Development	Assay Transfer	Pilot Screen	Full Deck Screen + Confirmation	Medicinal Chemistry

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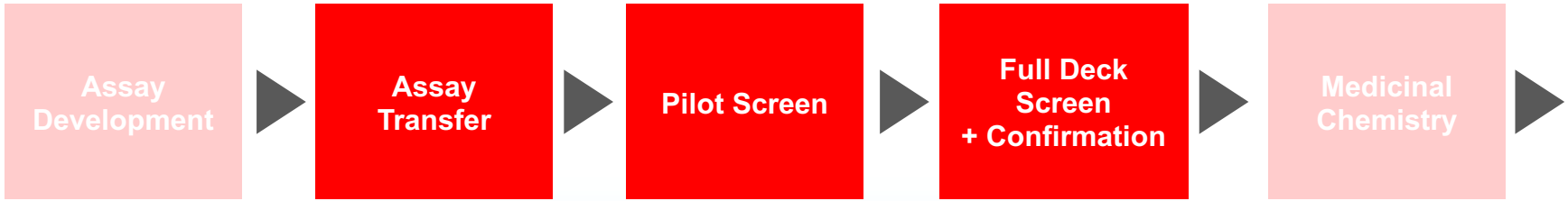

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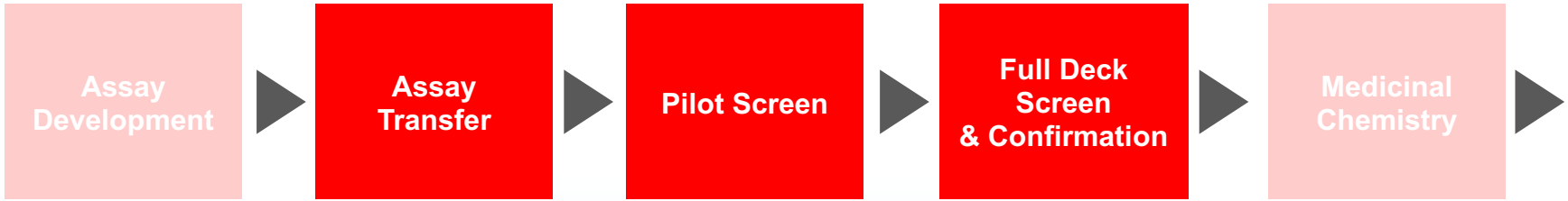
The National Drug Discovery Centre



For assays ready to be transferred onto automated platform

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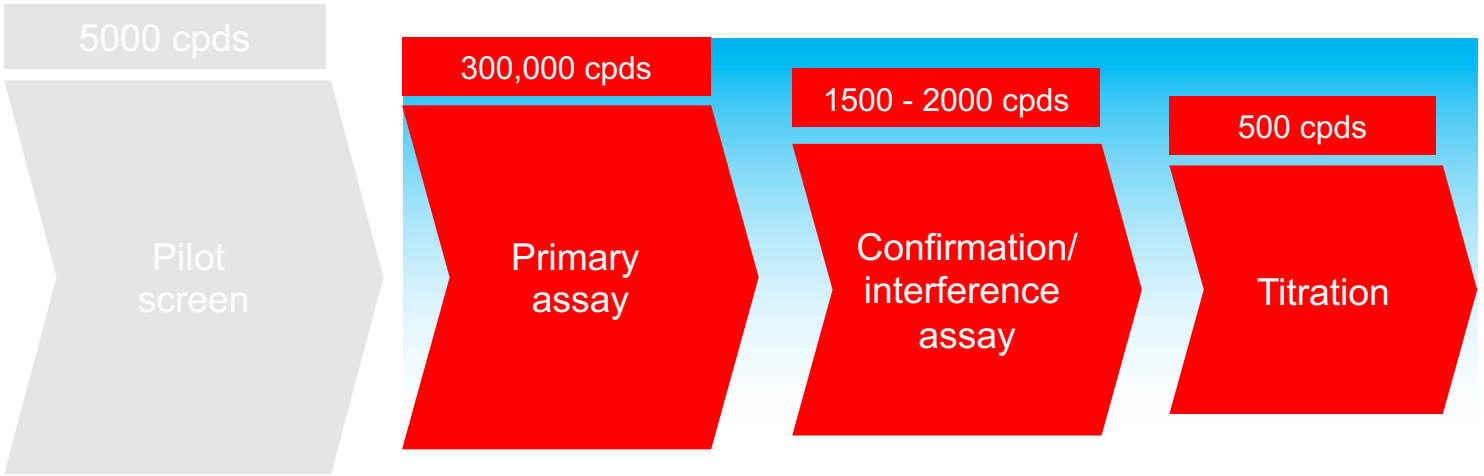
Medicinal chemistry for these projects not included in NDDC

You decide how to proceed

Screening process



- 1 concentration (single-point)
- Remove false positives
- IC_{50} determination (titration curve)

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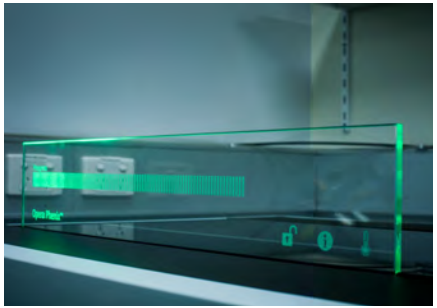
Screening lab assets

Team



Libraries

Software & Database

Robotics & Instruments

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Our team

- The team has more than 100 years of combined experience
- Automation, engineering, data analysts and screening experts from industry and academia
- Has grown from a 4-person team to 14 people today, with further growth over the next few years

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Major assay readouts & technologies

Categories of assays

GPCR	Enzyme	Ion channel	Cell-based	Protein-Protein interaction

Types of assays

GPCR	Enzyme	Ion channel	Cell-based	Protein-Protein interaction
Ca2+ flux	ATP/ADP consumption (luminescence/FP)	Electrophysiology (patch clamp)	Homogenous ELISA, TR-FRET/AlphaLISA	AlphaScreen/ TR-FRET
IP-One, cAMP measurement TR-FRET	Cleavage of tractable substrate	Membrane potential measurement (fluorescent dye)	Flow cytometry	Fluorescence polarisation (FP)
Cellshape change (impedance)	Alpha reagent / FRET or TR-FRET assay		Viability assay	
			High content imaging	

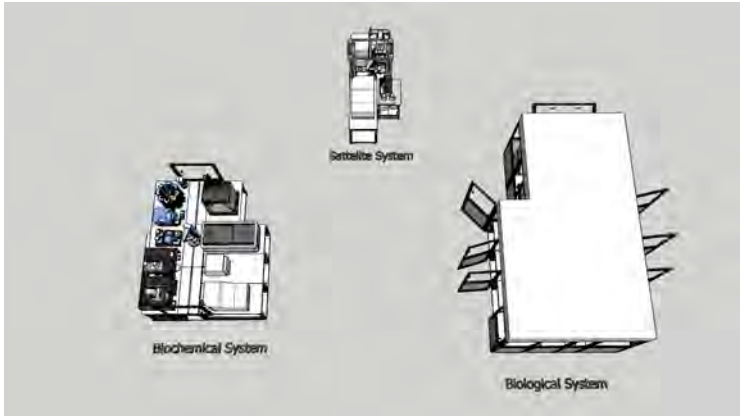
Coming soon | Basic technology | Recently implemented

Readers

- High Content : PE Opera phenix
  - confocal imaging with high throughput through simultaneous acquisition
- Multimode reader: BMG PHERAstar FSX
- Automated FACS: Intellicyt iQue Screener PLUS

Highly modular system

Each reader is movable and can be installed on the three different platforms according to the assay requirements:



Optimisation of equipment use: When not integrated in platforms, readers can be used as stand-alone

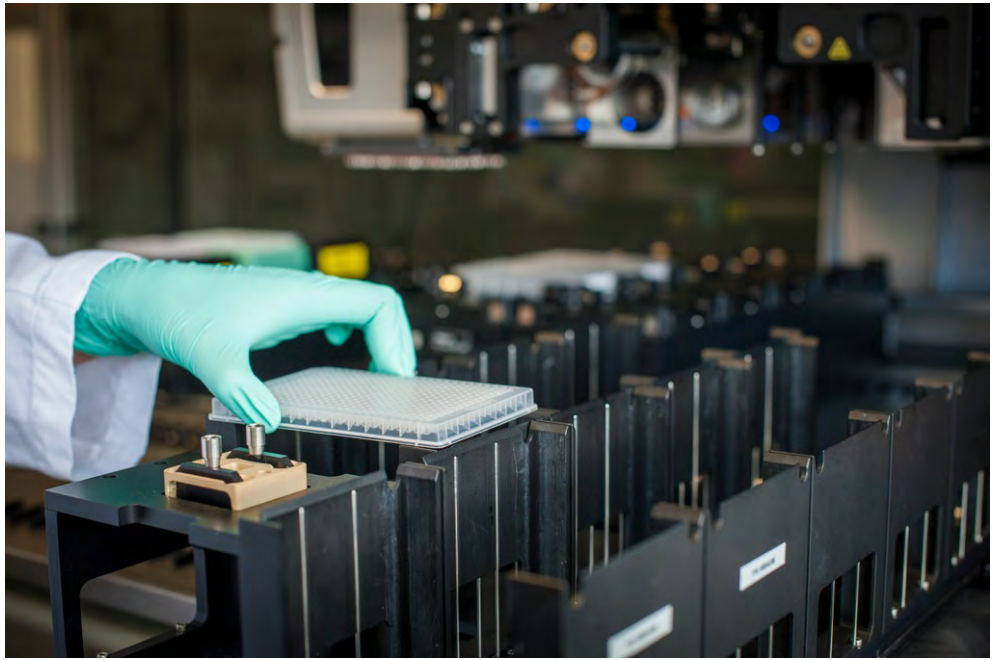
Customisation of the platform according to our needs

Efficiency: Assay development and screen will be run on the same instrument, minimising the assay transfer time

Scalable integration that could easily incorporate new technologies

Your screening assay

- You provide the assay and specific materials (e.g. cell lines, proteins)
- Must meet minimum requirements:
  - Demonstrated in 96-well format with:
    - minimum robustness
    - signal-to-background
    - component-stability requirements



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What we offer

- Fully staffed facility with drug screening expertise
- Latest in advanced robotic high-throughput screening
- Researchers from eligible Australian research institutions can apply for a **subsidised screen at a 90% discount**

What you get

Detailed report with:

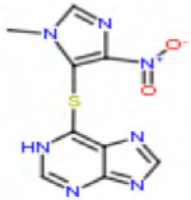
SOP

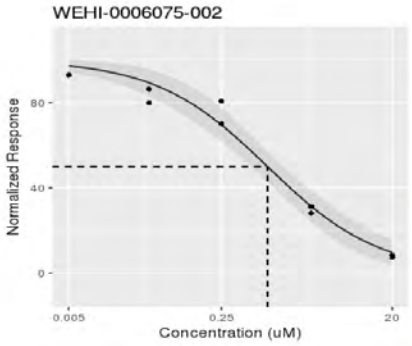
Screening campaign results

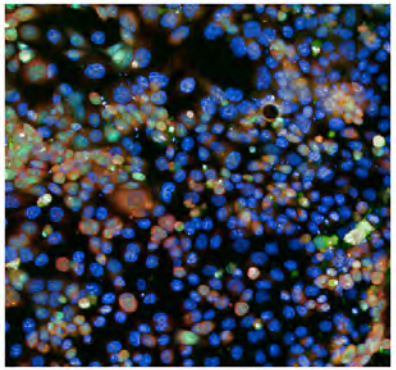
Hit list with:

- Structure of the hits
- IC_{50}
- Supplier information (vendor, catalogue ID)

Intellectual property is fully owned by you







What will it cost?

- Full cost of a 300,000-compound screen at the facility is typically in the range of $1.00 to $1.50 per compound. (i.e. $300,000 - $450,000)
- Indicative pricing with a 90% subsidy is $30,000 - $45,000
- Half of this fee is payable upfront, with the balance upon receipt of the final report.

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How to apply

- Visit the NDDC website to get further information: **nddc.wehi.edu.au**
- To obtain access (username and password) to the online application portal, please contact us on: **nddc@wehi.edu.au**
- Login to the secure online applications portal
- Fill out and submit the required documentation
- Applications close 7 November

How are projects selected?

- Applications reviewed by an expert panel
  - With expertise in biological sciences, translational biology and drug discovery
  - Assembled from Australian and international research organisations

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National Steering Committee

Voting members

- Professor Simon Foote (Chair, Emeritus Professor, John Curtin School of Medical Research)
- Professor Michael Parker (Director, Bio21 Institute, University of Melbourne)
- Professor Susan Charman (Director, Centre for Drug Candidate Optimisation)
- Professor Liz Hartland (Head, Department of Molecular and Translational Sciences, Monash University)
- Dr Dennis Liotta (Executive Director, Emory Institute for Drug Development, Emory University)
- Dr Andrew Harvey (Senior Director, QEDDI)
- Dr Lorna Mitchell (Senior Project Lead, BioCurate)
- Professor Murray Norris (Deputy Director, Children's Cancer Institute)
- Professor Peter Klinken (Chief Scientist of Western Australia)
- Associate Professor Sandra Nicholson (Laboratory Head, Inflammation Division, Walter and Eliza Hall Institute)
- Professor Nick Nicola (Laboratory Head, Blood Cells & Blood Cancer Division, Walter and Eliza Hall Institute)
- Professor Peter Colman (Laboratory Head, Structural Biology Division, Walter and Eliza Hall Institute)

Project selection

- Key selection criteria
  - Scientific quality and rationale
  - Feasibility
  - Innovation
- Two screens will be selected in the first round, four in the second round
  - Capacity will grow to 16 screens per year

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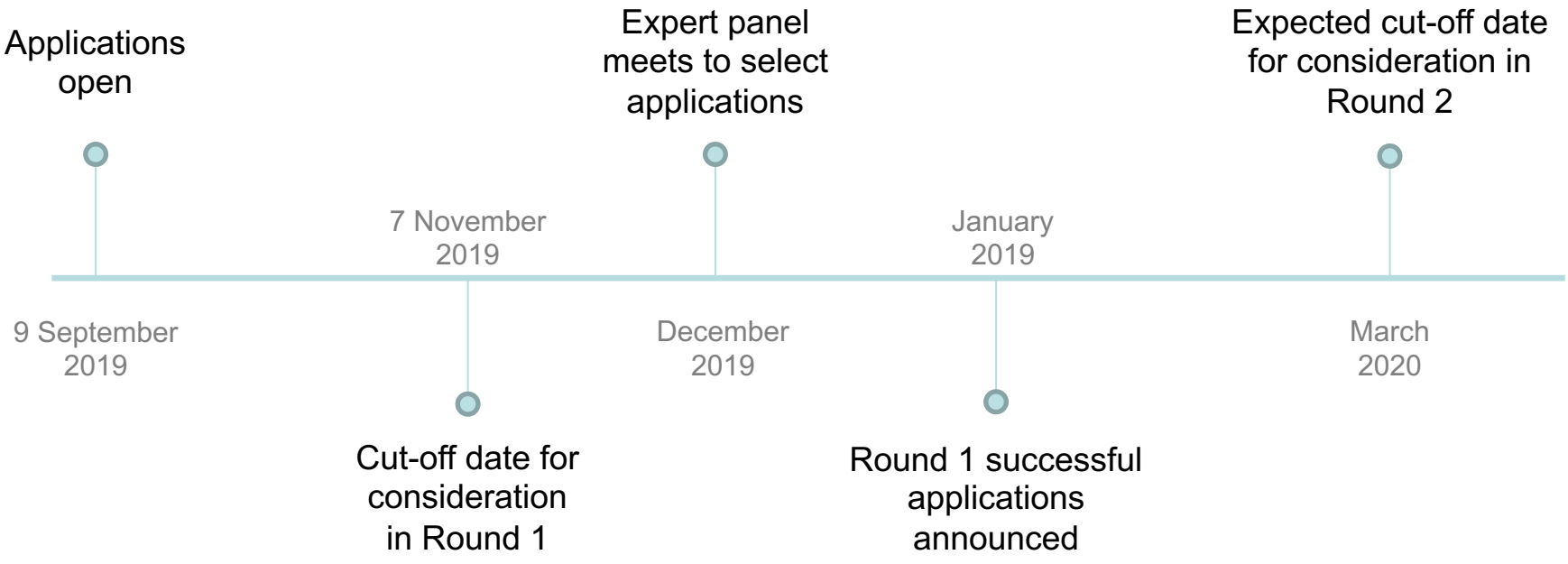
Applications timeline



Confidentiality

- Your data and project ideas will be treated confidentially and securely
- Applicants should visit **nddc.wehi.edu.au** to download the Mutual Confidentiality Agreement template.
  - Please sign the agreement before submitting confidential information.
- Except for the **Project title** and **Non-confidential lay summary**, all sections of your application will be treated as confidential.

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Who should you contact

Key team members

- **Jeff Mitchell**
  Acting Program Manager, NDDC
- **Helene Jousset**
  Head of Screening Laboratory
- **Kym Lowes**
  Deputy Head of Screening
- **Guillaume Lessene**
  New Medicines and Advanced Technology Theme Head

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Starting on the drug discovery journey

If you have identified the key role of a novel protein target in disease development, and

- You would like to develop a compound that targets this protein:
  - To develop a novel medicine, or
  - To develop a chemical probe to further validate the biology of this target

OR

If you want to screen directly on cells (cell lines, organoids and primary cells), and

- You have engineered cell lines that report on a phenotype, or
- You would like to identify compounds that target a pathway in cells

Contact us

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Funders & donors

Australian Government
Department of Health

Australian Government
Department of Industry, Innovation and Science

- Mike Fitzpatrick AO and Helen Sykes
- Anonymous

VICTORIA State Government

AWM ELECTRICAL & DATA SUPPLIERS

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Thank you

Happy to answer your questions

nddc.wehi.edu.au

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