COVID-19 Vaccines and Treatments: State of Play (12 July 2020)

Vaccines:

- There are currently over **190** vaccine candidates in development, including **17** in clinical trials.
- Five have conducted/are conducting clinical trials in Australia:
  - **Inovio Pharmaceuticals** DNA vaccine (INO-4800) from the US (*Operation Warp Speed* & *CEPI*)
    - Interim data from 40 participants of a Phase I clinical trial to test the safety and immunogenicity indicated the vaccine was well tolerated and generated appropriate immune responses. The data is not yet peer reviewed or published.
    - Pre-clinical research results have been peer-reviewed and published, demonstrating the vaccine in mice and guinea pigs induced functional antibody and T-cell immune responses. The animals were not challenged with SARS-CoV-2 to determine whether the vaccine was protective against infection.
    - Inovio has reportedly signed an agreement with German manufacturer Richter-Helm BioLogics for large-scale production.
    - An Inovio vaccine candidate for Middle Eastern Respiratory Syndrome was found to be well tolerated and effective in producing antibodies when trialled for protection.
  - The **Novavax** protein vaccine (NVX-CoV2373) from the United States (*Operation Warp Speed* & *CEPI*)
    - Novovax manufacturing (US)
    - Phase I trials are being conducted at Brisbane and Melbourne sites. Phase II trials are to be conducted in multiple countries, including the USA.
    - On 27 May 2020 Novavax announced the acquisition of a biologics manufacturing facility in Czech Republic.
    - Pre-clinical data demonstrated the vaccine induced antibodies that block the receptor required for viral entry into human cells (ACE2) and antibodies that neutralise SARS-CoV2 in baboons and mice. In mice the vaccine protected against

SARS-CoV2 infection with no evidence of vaccine associated enhanced respiratory disease. This data is at pre-print stage and is not yet peer reviewed.

- The **Clover Biopharmaceuticals** protein vaccine (S-Trimer) from China (*CEPI*)
    - Clover manufacturing (China)
    - Perth-based Linear Clinical Research conducting the Phase I trial and the Harry Perkins Institute are seeking expressions of interest.
    - Clover Biopharmaceuticals has partnered with Dynavax and GSK to trial its vaccine with adjuvants CpG 1018 and AS03 respectively.
- The **University of Queensland (UQ)** protein vaccine (UQ-1-SARS-CoV-2-Sclamp) from Australia (*CEPI*)
    - Licenced to manufacture by CSL (Australia).
    - Funding: $5m from Medical Research Future Fund (MRFF), $10 million from the QLD Government and $3.5 million from the Paul Ramsay Foundation.
    - Phase 1 planned to start this week.
    - If clinical trials are successful, the vaccine is expected to be available in 2021.
- **Flinders University (SA) / Vaxine** recombinant protein-based vaccine (COVAX19) from Australia
    - A Phase 1 clinical trial will test 40 healthy candidates and results are expected in six to eight weeks.
    - Announced a partnership with Sypharma (Australia) and Medytox Inc. (Korea) to progress vaccine development and commercialisation.

- Other candidates being monitored include:
    - The **University of Oxford** viral vector vaccine (AZD1222) from the United Kingdom (*Operation Warp Speed* & *CEPI*)
        - Licenced to manufacture by AstraZeneca (US, Europe)
        - A phase 2/3 clinical trial aiming to determine the efficacy, safety and immunogenicity, aiming to recruit 10,260 healthy participants.
        - Published pre-clinical studies demonstrated a single vaccination of six rhesus macaques (a non-human primate model) significantly reduced viral replication

and prevented lung damage following infection with SARS-CoV-2. The data was published prior to peer review to share timely data and assist the public health response to COVID-19.

- The **Moderna** mRNA vaccine (mRNA-1273) from the United States (*Operation Warp Speed* & *CEPI*)
    - Moderna manufacturing, along with Lonza globally (in US and Switzerland first)
    - Fill and finish manufacturing by Catalent biologics facility in US
    - Preliminary results of Phase I trial in 45 study participants the vaccine was generally well-tolerated and induced SARS-CoV-2 specific antibodies. Results released from 8 participants suggests the vaccine induced virus-neutralising antibodies, however the data is not yet peer reviewed or published.

Treatments:

- As at 8 July 2020, **1265** clinical trials relating to COVID-19 have been registered with the World Health Organisation's (WHO) International Clinical Trials Registry Platform.
- Some treatments being monitored include:
    - **Remdesivir**
        - The Therapeutic Goods Administration (TGA) has granted provisional approval to remdesivir ("Veklury", Gilead Sciences Pty Ltd) as the first treatment option for COVID-19. It has received provisional approval for use in adults and adolescent patients with severe COVID-19 symptoms who have been hospitalised.
        - Remdesivir is the most promising treatment option so far to reduce hospitalisation time for those suffering from severe coronavirus infections.
        - Remdesivir will not be available to Australians unless they are severely unwell, requiring oxygen or high level support to breathe, and in hospital care.
    - **Dexamethasone**
        - On 16 June 2020 the Chief Investigators of the Trial released a statement regarding results for 2104 patients that were randomised to receive 6mg dexamethasone daily for 10 days compared with 4321 controls. The preliminary results indicate that the drug reduced mortality in critically ill COVID-19 patients:
            - In ventilated patients mortality was reduced by one-third

    - In patients receiving oxygen mortality was reduced by one-fifth
    - There was no benefit in patients with mild disease.
  - The Australian National COVID-19 Clinical Evidence Taskforce has released a statement that once the peer-reviewed data from the study are available, the Taskforce will incorporate evidence into the clinical guidelines.

- **Chloroquine or Hydroxychloroquine**

  - The Australian National COVID-19 Clinical Evidence Taskforce has a strong recommendation against use. Adding:
    - For people with COVID-19, only administer hydroxychloroquine in the context of randomised trials with appropriate ethical approval.
  - The RECOVERY trial stated on 5 June that no clinical benefit from using hydroxychloroquine in hospitalised patients with COVID-19 was found.
  - On 4 July WHO announced the hydroxychloroquine treatment arm of the Solidarity Trial had been discontinued with immediate effect.

- **Lopinavir/Ritonavir**

  - The Australian National COVID-19 Clinical Evidence Taskforce notes the release of the press statement from the chief investigators of the RECOVERY trial on 29 June that found no clinical benefit from using lopinavir-ritonavir in hospitalised patients with COVID-19.
  - On 4 July WHO announced the lopinavir-ritonavir treatment arm of the Solidarity Trial had been discontinued with immediate effect. The Taskforce is awaiting publication of the results of both trials.