ASX ANNOUNCEMENT 29 March 2021

Cynata Expands MEND clinical trial in COVID-19 and Respiratory Failure

Melbourne, Australia; 29 March 2021: Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that it has received ethics committee approval to expand recruitment criteria in its active MEND (MEseNchymal coviD-19) clinical trial.

Key highlights

- **Ethics committee approval received to expand the recruitment criteria of Cynata's MEND clinical trial in patients in intensive care with respiratory failure, to include other causes beyond COVID-19 (such as influenza)**
- **The MEND trial will investigate early efficacy of Cymerus MSCs in patients with respiratory failure, who meet the well-established criteria for Acute Respiratory Distress Syndrome (ARDS)**
- **The trial expansion increases the pool of eligible patients, and is therefore expected to significantly accelerate recruitment**
- **Respiratory failure/distress (including ARDS) is a severe and life-threatening illness, representing a major unmet medical need**

The MEND clinical trial was initially designed to investigate early efficacy of Cynata's proprietary Cymerus™ mesenchymal stem cells (MSCs) in adults admitted to intensive care with COVID-19. The approved expansion will enable recruitment of patients with respiratory failure arising from other causes, with COVID-19 no longer a requirement. In view of the current state of control of the COVID-19 pandemic in Australia, this expansion of recruitment criteria is expected to substantially increase the pool of potential subjects for the trial.

The MEND trial is an open-label, randomised controlled clinical trial to investigate early efficacy of Cymerus MSCs in patients with respiratory failure. Cynata is seeking to enrol 24 adult patients admitted to intensive care with respiratory distress (or compromised lung function) at selected hospitals in Australia.

A corporate presentation on the MEND clinical trial and respiratory distress is attached to this announcement.

Dr. Kilian Kelly, Cynata's Chief Operating Officer, said:
"The expansion of this clinical trial represents execution of our strategy to ensure that, despite the dynamics of the COVID-19 pandemic, we will substantially increase the catchment of patients to accelerate the completion of the MEND trial. We have developed a solid pre-clinical data set in relevant diseases models of the severe respiratory distress and associated complications suffered by many patients affected by respiratory viruses such as SARS-CoV-2 (the virus that causes COVID-19) and influenza. This expansion will increase the number of patients eligible for recruitment into this trial, which is designed to investigate the potential benefits of our MSCs in treating these severely ill patients."

-ENDS-

Authorised for release by Dr Ross Macdonald, Managing Director & CEO

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About Cynata Therapeutics (ASX: CYP)

Cynata Therapeutics Limited (ASX: CYP) is an Australian clinical-stage stem cell and regenerative medicine company focused on the development of therapies based on Cymerus™, a proprietary therapeutic stem cell platform technology. Cymerus™ overcomes the challenges of other production methods by using induced pluripotent stem cells (iPSCs) and a precursor cell known as mesenchymoangioblast (MCA) to achieve economic manufacture of cell therapy products, including mesenchymal stem cells (MSCs), at commercial scale without the limitation of multiple donors.

Cynata's lead product candidate CYP-001 met all clinical endpoints and demonstrated positive safety and efficacy data for the treatment of steroid-resistant acute graft-versus-host disease (GvHD) in a Phase 1 trial. Clinical trials of Cymerus MSC products in osteoarthritis (Phase 3) and in respiratory distress (Phase 2) are currently ongoing. Planning is also underway for further clinical trials of Cymerus MSC products in GvHD (through licensee Fujifilm), critical limb ischemia, idiopathic pulmonary fibrosis, renal transplantation, and diabetic foot ulcers. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of numerous diseases, including the clinical targets mentioned above, as well as asthma, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.

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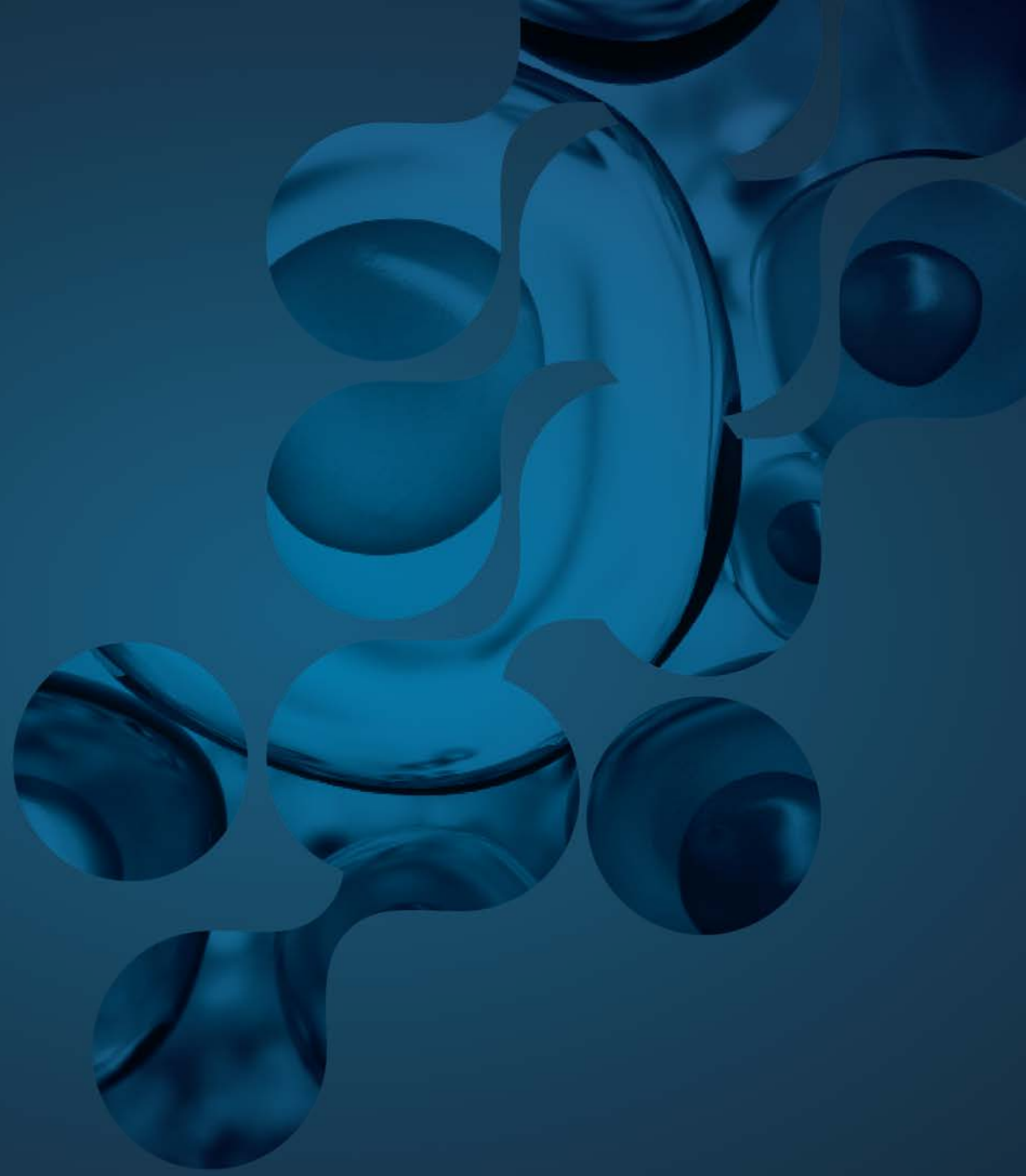
A Next Generation Stem Cell Therapeutics Company

MEND Clinical Trial Update: Cynata Therapeutics Limited

March 2021



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MEND Clinical Trial Update

MEND Phase 2 clinical trial recruitment criteria expanded: patient recruitment to target 24 subjects admitted to ICU with respiratory failure (COVID-19 is no longer a restriction[1])

Focus to be on ICU patients with **respiratory failure;** expected to **increase the pool** of eligible patients

Trial outcomes may have potential relevance in ARDS[2], CRS[3] and sepsis

1. Original recruitment criteria was respiratory distress and expected COVID-19 or a COVID-19 diagnosis. 2. Acute Respiratory Distress Syndrome. 3. Cytokine Release Syndrome

MEND[1] | Amended Phase 2 clinical trial

Ethics approval obtained to expand patient population to increase the pool of potential subjects

Target population

- 24 adult patients admitted to intensive care with **respiratory failure** (compromised lung function)
- Respiratory Failure is a collection of signs and symptoms which collectively can be known as Acute Respiratory Distress Syndrome (ARDS), with significant overlap in patients experiencing CRS and sepsis

Study design

- In collaboration with CPA Research Institute[2] and COVID-19 Stem Cell Treatment Group
- Open-label, randomised controlled clinical trial based in NSW, Australia
- Twelve patients randomised to receive Cymerus MSC infusions with standard care; twelve patients randomised as the control group, to receive current standard of care
- Primary endpoints: an improvement in PaO_2 / FiO_2 ratio (oxygenation of the patients blood) and safety & tolerability, up to Day 28

Key milestones

- ✓ Ethics committee approval obtained for original trial protocol
- ✓ Trial start-up activities completed[3]
- ✓ Patient enrolment open
- ✓ Ethics committee approval received to expand recruitment criteria beyond COVID-19
- ❑ Seeking to enrol 24 adult patients admitted to intensive care with respiratory distress

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1. MEseNchymal coviD-19 Trial (MEND)
2. CPA = Cerebral Palsy Alliance
3. Document preparation; Electronic case report form, study database & safety monitoring systems; Study team training; Research Governance Office approval at each study site; Import, store & distribute Cymerus MSC product

Initial rationale underpinned by potential utility of MSCs in COVID-19

Rapid program planning and approval driven by increased market interest and Cynata's strong pre-clinical data in key target indications commonly arising from a severe case of COVID-19

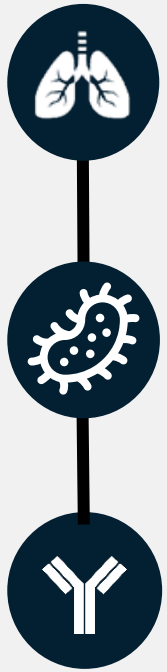
Increased global interest in the potential of MSCs to treat complications of COVID-19[1]

In some patients, COVID-19 causes **severe complications, particularly involving the lungs**

ARDS, sepsis, and CRS are all common hallmarks of serious cases of COVID-19

Cynata leveraged its pre-clinical data and increased interest to accelerate development with relevance to multiple indications

Underlying target indications present significant unmet needs *beyond* COVID-19:



Acute Respiratory Distress Syndrome (ARDS)

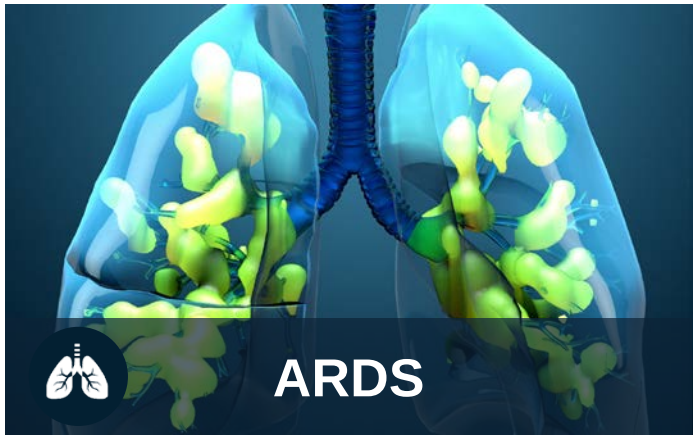
Sepsis (also known as blood poisoning)

Cytokine Release Syndrome (CRS)

Note: MSCs are not inherently antiviral and are not a vaccine.
1. Early studies demonstrating potential utility (source: Leng, G. et al., Aging & Disease, 11: 216 April 2020)

Target indications represent significant unmet medical needs

ARDS, sepsis and CRS are manifestations of an excessive inflammatory response and often occur in patients simultaneously



Disease	**Inflammatory process leading to build-up of fluid in the lungs** due to infection, trauma and inhalation of noxious substances. There are currently no specific treatment options.	Over-reaction of the immune system to infection, known as **blood poisoning**. Existing treatment options are currently limited.	A potentially **severe and life-threatening immune response,** caused by a large, rapid release of cytokines into the blood, which can be a response to a virus[5] or an adverse reaction to cancer immunotherapy.
Unmet Need	▪ Accounts for **10% of all ICU admissions**; ▪ **~25%** of patients require mechanical ventilation ▪ Results in **hospital mortality of up to 46%[1].**	▪ Sepsis affects **~49m** people worldwide p.a. ▪ Leading up to **11m deaths[3]** ▪ Making it the **most common cause of death** in hospital ICUs	Treatment of CRS in cancer patients could significantly **limit the effectiveness of their cancer treatment**, which could otherwise be curative.
Market Opportunity	**Combined market opportunity of ~US$8.4bn[2,4,6]**		

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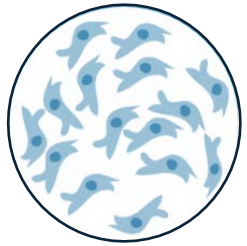
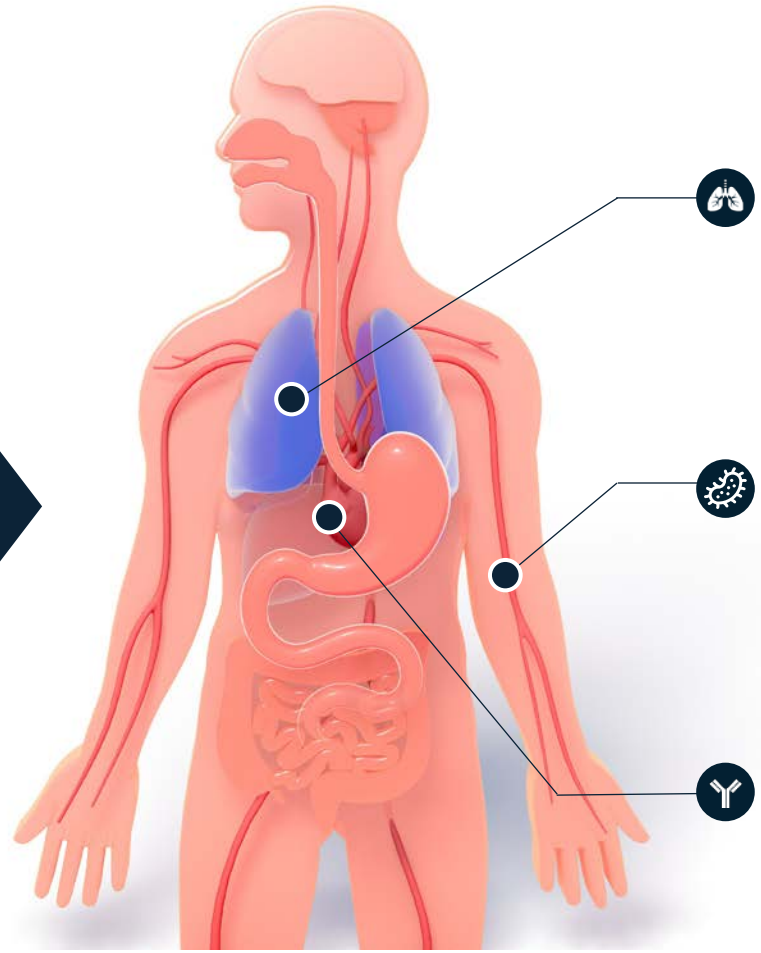
1. Bellani G, Laffey JG, Pham T, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. Jama. 2016;315(8):788; 2. Vasomune Therapeutics company announcement, 2018 (Reflects total global market opportunity in 2018) 2. Vasomune Therapeutics company announcement, 2018 (Reflects total global market opportunity in 2018). 3. World Health Organisation, 2020 https://www.who.int/news-room/fact-sheets/detail/sepsis 4. GlobalData 2017 (Reflects total global market opportunity in 2026) 5. Mortality in COVID-19 patients has been linked to the virus inducing a 'cytokine storm'; excessive production of proinflammatory cytokines leads to ARDS aggravation and widespread tissue damage, leading to organ failure and death. (Source: Ragab D et al. (2020) The COVID-19 Cytokine Storm; What We Know So Far. Front. Immunol. 11:1446. doi: 10.3389/fimmu.2020.01446) 6. GlobeNewswire, 2020

Cymerus MSCs show positive effects in preclinical studies

Cynata's MSCs have shown potential as treatments in preclinical studies, including reducing inflammation which could be extremely useful in the MEND trial addressing the inflammatory reaction in these patients



Cymerus MSC treatment administered intravenously to patient in the MEND trial



Outcomes from Cynata preclinical studies: foundation for the evaluation in adult patients in the MEND clinical trial

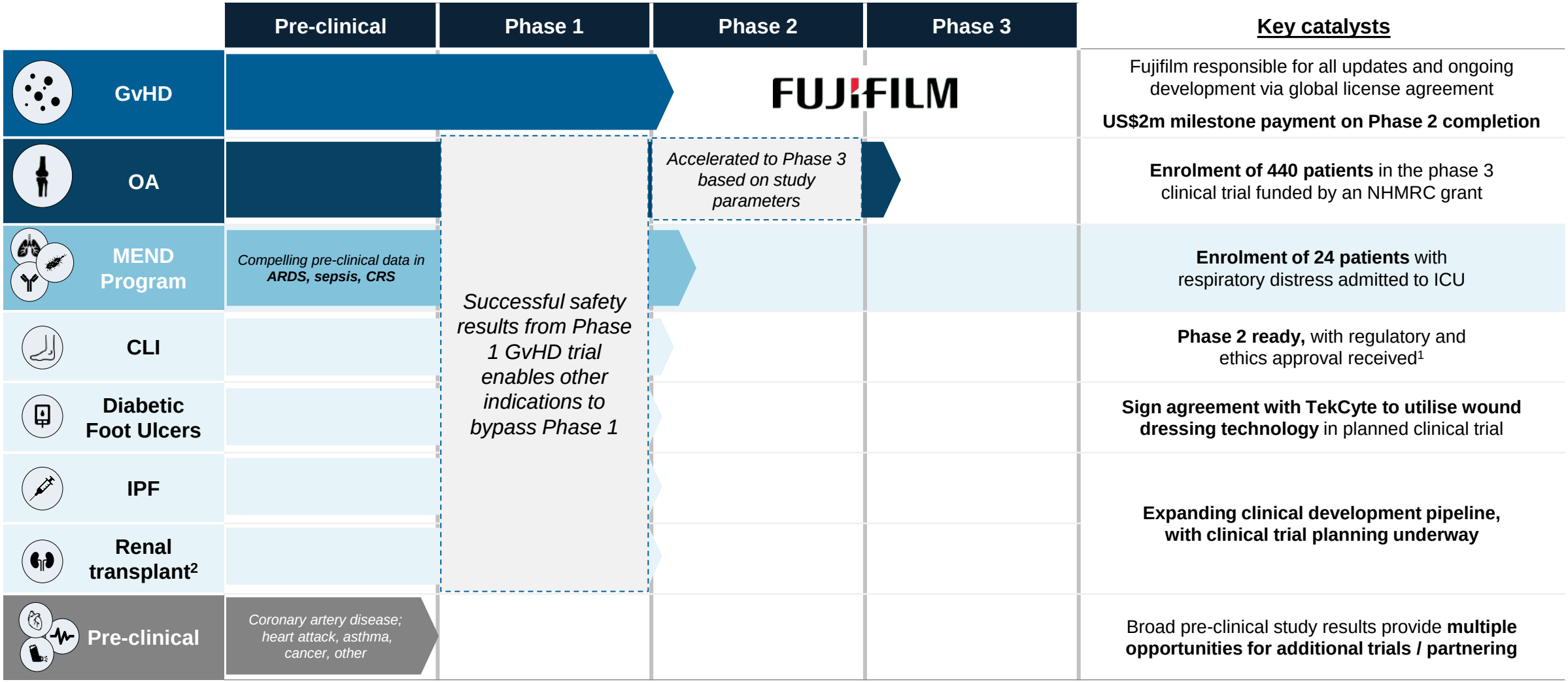
ARDS
- Reduction in inflammation
- Reduction in severity of lung injury
- Reduction in severity of circulatory shock (life threatening)

Sepsis
- Decreased inflammation
- Increased blood oxygen levels
- Decreased barrier permeability (prevents harmful proteins entering the lungs)
- Reduced lung injury

CRS
- Reduced inflammation
- Substantial protection against CRS symptoms which can present in various body systems
- Improvements in body temperature

Development pipeline and outlook

Broad and advanced clinical development pipeline, with multiple active trials and near-term catalysts



Note: Timing is dependent on a number of external factors (including COVID-19 restrictions)

1. Trial timing uncertain due to continued impact on recruitment due to COVID-19, and being assessed as part of broader clinical development strategy
2. Preclinical model of organ transplant rejection complete

Key objectives for 2021

Cynata is in a strong position going forward with ~A$30m cash[1] to fund all planned clinical trials and advance development of its proprietary Cymerus platform technology

- Execute on the expansion of the clinical pipeline and commence new clinical trials
- **Executing strategy to accelerate recruitment in the MEND clinical trial**
- Advance recruitment progress in the active SCUlpTOR (OA) phase 3 clinical trial
- Optimise manufacturing capabilities to enhance scale-up efficiencies
- Execute US regulatory strategy, to drive commercialisation of its MSC products
- Continue engagement in partnering discussions, and actively pursue of new opportunities

Note: Timing is dependent on a number of external factors (including COVID-19 restrictions)
1. Cash as at 31 December 2020 (A$25m), adjusted for the proceeds of the entitlement offer and shortfall placement in Jan 21 (A$3.3m), and the R&D Tax Incentive Refund received in Feb 21 (A$1.4m)

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