PITT STREET RESEARCH

Noxopharm Ltd

Share Price: A$0.31

ASX: NOX

Sector: Healthcare

5 August 2020

Veyonda® firming up as an important novel immuno-oncology drug candidate

NOX confirms clinical benefit of Veyonda®

Since our initiation report published on 23 April 2020, NOX has made important progress in its aim of developing its lead drug, Veyonda®, as a ground-breaking form of treatment of late-stage cancers. The first step was to test Veyonda in men with metastatic castration-resistant prostate cancer (mCRPC). The results of the DARRT-1 study were announced on 30 April 2020 and revealed that an immune response known as an abscopal response was achieved in a high proportion of mCRPC patients following a combination of Veyonda® and low-dose radiotherapy. The clinical study demonstrated that 27% (4/15) patients with mCRPC experienced a shrinkage of both irradiated and non-irradiated tumours following the DARRT therapy, which in our view is a remarkable result given how rare abscopal responses occur in medical therapy.

Pre-clinical data backs this benefit being due to key immuno-oncology effect

Laboratory data has now provided an explanation for this clinical effect with evidence that, idronoxil (IDX), the active ingredient in Veyonda works by activating cancer-fighting immune cells (T-cells) and causing them to infiltrate tumours and kill cancer cells. This effect is known as converting COLD tumours to HOT tumours and given that a drug that does this is a major goal of the global pharmaceutical industry, we expect this discovery to lead to growing industry interest in NOX.

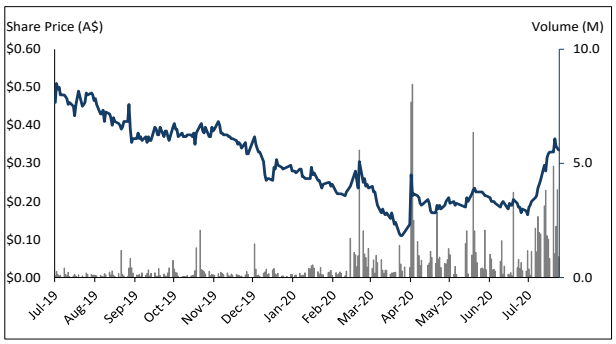
NOX to commence COVID-19 Phase 1 trial in Europe

Also, in April 2020, NOX announced its intention to evaluate the use of Veyonda® in COVID-19 patients who are at risk of multi-organ failure and acute respiratory distress syndrome (ARDS). This is based on the discovery that one of the drug's anti-cancer actions is to block an important function of cancer cells known as STING signalling. This same signalling pathway is thought to be behind the cytokine storm damaging and even killing COVID-19 patients with poor lung function upon organ damage initiation. Veyonda is on track to enter a Phase 1 clinical trial in Europe starting Q3 2020 with the aim of confirming safety and proof-of-principal of Veyonda.

Market Cap. (A$ m)	65.0
# shares outstanding (m)	213.2
# shares fully diluted	244.0
Market Cap Ful. Dil. (A$ m)	75.6
Free Float	64.5%
52-week high/low (A$)	0.47 / 0.09
Avg. 12M daily volume ('000)	656.7
Website	www.noxopharm.com

Source: Company, Pitt Street Research

Share price (A$) and avg. daily volume (M, r.h.s.)



Source: Thomson, Pitt Street Research

Valuation metrics	
DCF fair valuation range (A$)	0.42 – 0.89
WACC	13.5%
Assumed terminal growth rate	-3% to -5%

Source: Pitt Street Research

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Veyonda® is a potential COVID-19 drug candidate

NOX proposed to evaluate the use of idronoxil in COVID-19 patients

In April 2020, NOX proposed to evaluate the use of idronoxil (IDX) in COVID-19 patients who are at risk of multi-organ failure and acute respiratory distress syndrome (ARDS).

Initially, NOX proposed to use an oral dosage formulation of IDX called NOX-19 in patients showing early signs of organ damage, with the aim to have fewer patients needing to be admitted to the Intensive Care Unit (ICU) and a reduced need for ventilators. However, given the fact that Veyonda, NOX's leading drug candidate, has already achieved Investigational New Drug (IND) status in the US and holds potential to treat COVID-19 patients, the company will instead proceed with Veyonda.

Impact of COVID-19 on human body

The real risk for COVID-19 patients lies in the virus's progression from a mild disease into a more serious form characterised by respiratory failure, multi-organ failure, clotting problems and septic shock. End-stage treatment is limited to the usage of antibiotics and ventilators. At this stage, there is no cure for COVID-19. Death trend is also persisting.

Most deaths in COVID-19 patients are believed to be due to septic shock, a condition associated with inflammatory and clotting problems and believed to be contributing to multi-organ failure.[1]

When a patient becomes infected with COVID-19, his or her body's immune system is alerted to the presence of an invading virus by triggering the production of cytokines to fight the virus. One of the key pathways involved in that process is called STING (Stimulation of Interferon Genes) signalling pathway, which contributes to the recovery of most of COVID-19 patients. However, in a small portion of patients who develop breathing problems leading to low oxygen levels, self-DNA release upon organ damage gets detected by the STING signalling pathway, which then becomes hyper-active, triggering an excessive inflammatory reaction known as a cytokine storm, amplifying existing tissue damage and inducing blood clotting problems.[2,3] Eventually, this leads to self-destruction of major organs in the septic shock process as described above.

How does Veyonda® potentially mitigate COVID-19 deaths?

Veyonda® offers the potential of reducing the severity of septic shock and the number of COVID-19 patients dying from it, or even preventing it altogether

In April 2020, NOX announced that IDX, the active ingredient in Veyonda®, exerts an anti-inflammatory action through inhibition of the STING signalling pathway. NOX believes that by inhibiting the STING signalling pathway, the progression of cytokine storm could be blocked at its roots, which in turn will prevent the worsening of ARDS and multi-organ failure. Hence, Veyonda® offers the potential of reducing the severity of septic shock and the number of COVID-19 patients dying from it, or even preventing it altogether.

NOX to commence COVID-19 Phase 1 trial in Europe

On 19 June 2020, NOX announced the initiation of a Phase 1 trial (NOXCOVID-1) in COVID-19 patients in Europe. The aim of NOXCOVID-1 is to confirm the safety of Veyonda® in patients at risk of septic shock and the effectiveness of Veyonda® to inhibit or considerably reduce the development of cytokine

[1] Zhou et al. (2020). Clinical course and risk factors for mortality of patients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet, 395(10229):1054–1062. https://doi.org/10.1016/ S0140-6736(20)30566-3. https://www.ncbi.nlm.nih.gov/pubmed/32171076
[2] Benmerzoug et al (2019). Self-DNA sensing in lung inflammatory diseases. Trends in Immunology, 40 (8). https://doi.org/10.1016/j.it.2019.06.001. https://www.ncbi.nlm.nih.gov/pubmed/31262653
[3] Zhang et al (2020). TMEM173 Drives Lethal Coagulation in Sepsis. Cell host and Microbe, 27(4): 556-570. https://doi.org/10.1016/j.chom.2020.02.004. https://www.ncbi.nlm.nih.gov/pubmed/32142632

storm contributing to the death of COVID-19 patients. The outcome of the NOXCOVID-1 study will help the company to decide whether or not to commit to the funding of a larger trial.

NOXCOVID-1 will be applied to approximately 40 COVID-19 patients who have been admitted to hospital for respiratory insufficiency. Clinical Accelerator, a UK-based contract research organisation, has been appointed to oversee the trial. Datapharm, an Australian-based company, will be the data processor.

The process of obtaining regulatory approval for NOXCOVID-1 is underway. Once it is obtained, NOXCOVID-1 will be conducted in Ukraine and Moldova where COVID-19 cases and deaths have been rising.

The data from the NOXCOVID-1 trial will inform the Company's decision to potentially conduct a clinical trial of Veyonda in the U.S. in patients with SARS-CoV-2 (COVID-19) infection.

Market Size and Competition

As of 30 July 2020, US recorded a total of approximately 4.5M confirmed COVID-19 cases, of which deaths comprised of 3% of total cases (153,000).[4] Currently, the daily confirmed COVID-19 deaths trend in the US has been volatile and trending upward.

How NOX's Veyonda® differentiates itself from its competitors is by blocking a broader range of cytokines at their roots (not just individual cytokines) through the inhibition of the STING signalling pathway

To date, there are a number of COVID-19 clinical trials being conducted with drugs inhibiting individual components of the cytokine storm such as interleukins-6 (IL-6) and tumour necrosis factor-alpha (TNF-alpha). The research outcomes will demonstrate the usefulness of blocking individual cytokines out of the large number involved in a cytokine storm. How NOX's Veyonda® differentiates itself from its competitors is by blocking a broader range of cytokines at their roots (not just individual cytokines) through the inhibition of the STING signalling pathway.

Given the large unmet demand for a COVID-19 treatment, we see significant upside potentials in NOX should it succeed in obtaining all the necessary regulatory approvals and successfully prove Veyonda® as a cytokine storm inhibitor.

How did the market react to NOX's potential COVID-19 treatment?

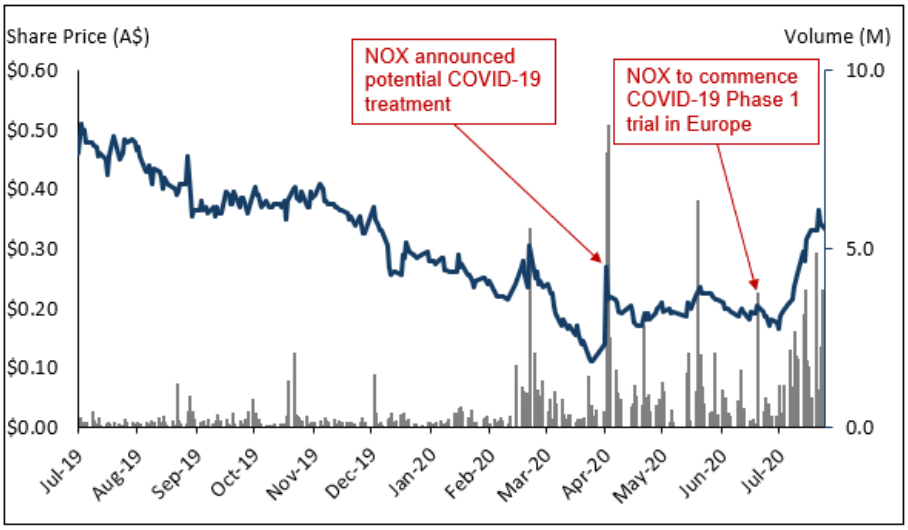
On 1 April 2020, when NOX proposed IDX as a potential treatment in COVID-19 patients, the stock price re-rated significantly from $0.14 per share to $0.27 per share (Figure 1). This implies that the market welcomed the news and believed in NOX's capability to treat COVID-19. In our view, the stock price reaction also highlighted the urgency of the pandemic as well as investors' eagerness in finding a treatment for COVID-19. Moreover, NOX's announcement on 19 May 2020 on the lodgement of its pre-IND submission to the FDA has further boosted investors' confidence, which in turn provided some support to the stock price.

In addition, investors also liked the news announced by NOX to commence its COVID-19 Phase 1 trial in Europe. Notably, the share price appreciated by almost 8% on 19 June 2020, the day when NOX made this announcement. Given the expedited nature of the regulatory approval process for COVID-19 clinical trial in Ukraine, we see this potential near-term regulatory approval as an important catalyst in driving another round of re-rate of the stock price. Furthermore, if the NOXCOVID-1 program can confirm proof-of-principle and safety of Veyonda® in COVID-19 patients and therefore progress into the next

[4] Source: Wikipedia: COVID-19 pandemic data.

larger trial study, we think there will be material upsides yet to be recognised by the market, the incorporation of which should result in considerable share price appreciation, in our view.

Figure 1: NOX share price chart



Source: Pitt Street Research, Company Reports

Oncology Programs

NOX demonstrates meaningful abscopal responses in end-stage prostate cancer patients

Following the successful completion of the Direct and Abscopal Response to Radiotherapy clinical program (DARRT-1) trial in December 2019, NOX has released details of the study in April 2020, delivering a meaningful abscopal responses rate in patients with late-stage metastatic castration-resistant prostate cancer (mCRPC).

As described in our initiation report, the company's NOX66 DARRT clinical program applies low dose radiation to trigger local inflammatory and immune responses in a single irradiated tumour, with Veyonda® designed to boost that response and extend it to all tumours in the body. The ultimate goal is to shrink both irradiated and non-irradiated tumours through a process known as the abscopal response, resulting in reduced pain and potentially improved survival.

Following DARRT therapy, 27% (i.e. 4/15) of patients with late-stage metastatic castration-resistant prostate cancer have experienced an abscopal response

Following DARRT therapy, 27% (i.e. 4/15) of patients with mCRPC have experienced an abscopal response. To the company's knowledge, this is the first time that anyone has been able to obtain a meaningful abscopal response rate in mCRPC. In our view, this is a big step achieved by NOX considering the very rare occurrence and benefits of abscopal responses.

Looking ahead, NOX plans to commence its DARRT-2 study, a Phase 2 trial, in early 2021. We believe the recent major benefit derived from a combination of Veyonda® and low-dose radiotherapy will make DARRT-2 an even more exciting study to look forward to.

NOX expands drug pipeline to include a new brain cancer treatment

In April 2020, NOX has expanded its drug pipeline program to incorporate an isoflavonoid drug that potentially treats a form of brain cancer known as glioblastoma multiforme (GBM).

GBM is an aggressive type of brain cancer that occurs mostly in people aged between 55-60. Globally, it is estimated that about 230,000 people die every year from brain and spinal cord cancers. GBM has a poor prognosis due to limited treatments and rapid tumour growth, with a survival rate of about 14 months following diagnosis.[5] Glutamate, the brain's main neurotransmitter chemical, is believed to be the key growth driver of GBM cells.[6]

NOX will now bring its new brain cancer drug candidate into a pre-clinical program

NOX's new isoflavonoid drug aims to inhibit the growth and proliferation of the cancerous GBM cells in the presence of glutamate. The company's recent proof-of-principal test results demonstrate that this is possible. NOX will now bring this new drug candidate into a pre-clinical program.

Given the significant unmet need in the treatment of brain cancer, we see immense upside potential in the company's isoflavonoid drug candidate. If NOX can successfully progress the new drug into clinical studies, we believe it will add considerable value to the company's drug portfolio.

NOX conserves cash through reduced burn rates

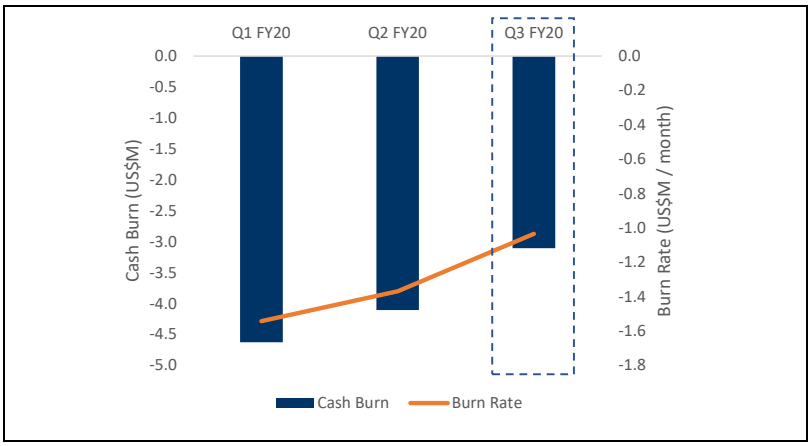
As provided in its 3Q20 result, NOX has demonstrated its ability to deliver an improved total cash outflow of $3.1M compared to $4.1M over the previous quarter. This was achieved through the reduction of staff and overhead costs.

Quarter-on-Quarter burn rates trending downwards, reflecting operational efficiency

Figure 2 compares NOX's cash burn quarter-on-quarter. Clearly, 3Q20 cash burn was substantially lower compared to the previous two quarters, which reflects the operational efficiency achieved by the company. Notably, NOX's burn rates have been trending downwards.

Given NOX has successfully raised approximately A$7.33M net as part of its rights issue program, the proceeds have helped the company to strengthen its balance sheet, and should allow NOX to fund its ongoing oncology programs as well as the clinical testing of Veyonda® as a potential COVID-19 treatment.

Figure 2: Quarterly cash burn & monthly burn rates



Source: Pitt Street Research, Company Reports

[5] Davis M E. (2016) Glioblastoma: Overview of Disease and Treatment. Clin J Oncol Nurs. 2016October 1; 20(5): S2–S8.
[6] Ventakamarani V et al. (2019) Glutamatergic synaptic input to glioma drives brain tumour progression. Nature 573:532-538

Reiterating initial valuation

Our probability-weighted DCF valuation range remains largely intact

We retain our initial assumptions used in a probability weighted DCF. We reiterate our valuation range of $0.42 per share base case and $0.89 per share optimistic case. At this stage, we have not included the company's new brain cancer program in our valuation model due to its pre-clinical status. When and if NOX successfully progresses its isoflavonoid drug candidate into clinical trials, we will look to include it into our valuation. We apply the same logic to NOX's Veyonda® as a potential COVID-19 treatment.

We see the following events as catalysts that will help to re-rate NOX's stock price towards our valuation range:

- Successful clinical results of NOXCOVID-1 program in Europe
- Commencement of the DARRT-2 study
- Grant of IND approval for an expanded clinical trial in the US
- Continuation of positive results from the ongoing LuPIN study
- Grant of Orphan Drug status and a Fast Track approval for sarcoma study
- Positive results from isoflavonoid's pre-clinical program

Risks for Noxopharm

Risks specific to NOX. We see four major risks associated with NOX as a company and as a listed stock.

- **Clinical risk**. There is a risk that Veyonda® may fail to meet the primary or secondary endpoints in the clinical studies.
- **Financial risk**. There is a risk that NOX may not be able to obtain sufficient funds in the US markets.
- **Timing risk**. Veyonda® clinical studies in mCRPC or other indications could take longer than expected.
- **Regulatory risk**. Regulatory decisions may slow down or stop the market authorisation process for Veyonda®.

Risks related to pre-revenue Life Science companies in general.

The stocks of biotechnology and medical device companies without revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character.

Since most biotechnology and medical device companies listed on the Australian Securities Exchange fit this description, the term 'speculative' can reasonably be applied to the entire sector.

The fact that the intellectual property base of most biotechnology and medical device lies in science not generally regarded as accessible to the layman adds further to the riskiness with which the sector ought to be regarded.

Caveat emptor. Investors are advised to be cognisant of the abovementioned specific and general risks before buying any biotechnology or medical device stock mentioned on this report, including NOX.

Please refer to www.pittstreetresearch.com for our initiation report on NOX.

Analyst qualifications

Cheng Ge, lead analyst on this report, is an equities research analyst at Pitt Street Research.

- Cheng obtained a B.Com in Finance and LL.B from University of New South Wales in 2013, and has passed all three levels of the CFA Program.
- Prior to joining Pitt Street Research, he has worked for several financial services firms in Sydney, where his focus was on financial advice.
- He joined Pitt Street Research in January 2020.

Stuart Roberts has been covering the Life Sciences sector as an analyst since 2002.

- Stuart obtained a Master of Applied Finance and Investment from the Securities Institute of Australia in 2002. Previously, from the Securities Institute of Australia, he obtained a Certificate of Financial Markets (1994) and a Graduate Diploma in Finance and Investment (1999).
- Stuart joined Southern Cross Equities as an equities analyst in April 2001. From February 2002 to July 2013, his research specialty at Southern Cross Equities and its acquirer, Bell Potter Securities, was Healthcare and Biotechnology. During this time, he covered a variety of established healthcare companies such as CSL, Cochlear and Resmed, as well as numerous emerging companies. Stuart was a Healthcare and Biotechnology analyst at Baillieu Holst from October 2013 to January 2015.
- After 15 months in 2015 and 2016 doing Investor Relations for two ASX listed cancer drug developers, Stuart founded NDF Research in May 2016 to provide issuer-sponsored equity research on ASX-listed Life Science companies.
- In July 2016, with Marc Kennis, Stuart co-founded Pitt Street Research Pty Ltd, which provides issuer-sponsored research on ASX-listed companies across the entire market, including Life Science companies.

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