Early success in Phase 3 clinical trial for FSGS

Share Price: A$0.30

ASX: DXB

Sector: Healthcare

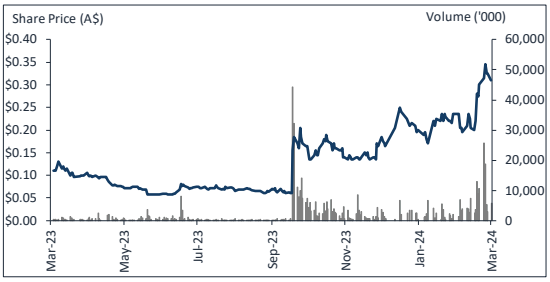
26 March 2024

Dimerix (ASX: DXB) is an ASX-listed biotechnology company focused on inflammatory diseases. Its flagship asset is DMX-200, is currently in a Phase 3 trial for a rare kidney disorder called focal segmental glomerulosclerosis (FSGS) and is the only such product to be in Phase 3 for FSGS, with no treatments on market.

Market cap. (A$m)	164.2
# Shares outstanding (m)	547.2
# Share fully diluted (m)	672.6
Market cap full. dil. (A$m)	201.8
Free float	72%
12-months high/low (A$)	0.370 / 0.052
Avg. daily volume ('1000)	2,297.5
Website	https://dimerix.com

Source: Company, S&P Capital IQ, Pitt Street Research

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



Source: S&P Capital IQ, Pitt Street Research

Encouraging interim Phase 3 results for DMX-200

On 11 March 2024, the company released results of the first interim analysis of the ACTION3 trial, and these showed positive results based on the proteinuria efficacy endpoint of the study. The analysis demonstrated that DMX-200 was performing better than placebo in reducing proteinuria and suggests that DMX-200 may result in improving kidney function when given to patients with FSGS already taking the standard of care background therapy. The positive results from the trial have paved the way to move ahead with Part 2 of the global study. Based on current recruitment rates, the outcome of the second interim analysis is expected around the middle of 2025 calendar year. This analysis will be more crucial as it is designed to capture evidence of both proteinuria and kidney function (as demonstrated by the Estimated Glomerular Filtration Rate (eGFR) slope), which may generate sufficient evidence to support conditional marketing approval.

Strategic partnerships will boost growth prospects

Dimerix has several near-term milestones awaiting it such as the execution of potential licensing deals for available jurisdictions, (including the US and China), and recruitment and dosing of 144 patients for Part 2 (the second analysis outcome is estimated for mid-CY25). Dimerix has also received non-binding term sheets for regional deals, with multiple parties in the data room conducting due diligence and negotiating a potential licensing agreement for several territories. If the trial is ultimately successful and the drug is taken to market, this will be the key catalyst for the creation of shareholder value. Dimerix is well poised to bring the drug to market with an existing commercial partner for Europe, Canada and ANZ in Advanz Pharma, and potentially more to come in jurisdictions not covered by Advanz Pharma.

Updated valuation range

We update our valuation of Dimerix to A$0.63 per share in a base case scenario and A$0.83 per share in an optimistic case scenario. We have reduced the discount rate in light of the company's results, but have also the increased the number of shares on issue after the recent capital raising. Please refer to pages 9-10 for more details on our valuation and the key risks to our thesis.

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Table of Contents

Re-introduction to Dimerix (ASX:DXB)

Dimerix is a biotech company, primarily focused on developing its proprietary product DMX-200 against Focal Segmental Glomerulosclerosis (FSGS). FSGS is the core focus at the moment, although DMX-200 may be applicable to other indications. Dimerix has another clinical stage asset in DMX-700 as well as a proprietary assay Receptor Heteromer Investigation Technology (Receptor-HIT), a scalable and globally applicable technology platform enabling receptor interactions for rapid screening and identification of new drug opportunities. Investors interested in more detail on DMX-700 and Receptor-HIT and how they work should see our initiation report from January, although we will briefly recap the company's future outlook with these assets later in this report.

What is DMX-200?

DMX-200 is an oral anti-inflammatory drug called repagermanium, administered to patients already taking the current standard of care (the blood pressure medication known as an ARB) for the treatment of kidney disease. It is administered as a single capsule twice daily to patients already on background standard of care treatment. ARBs, such as irbesartan and losartan, are the current standard of care treatment for kidney diseases generally. Irbesartan itself was formerly a blockbuster drug for Sanofi and Bristol-Myers Squibb, known as Avapro when it was approved by the FDA in 1997 for the treatment of hypertension.

How does DMX-200 work?

DMX-200 works as a blocker of the chemokine receptor 2 (CCR2) – the inflammatory pathway

DMX-200 blocks the chemokine receptor 2 (CCR2) pathway, which stops immune cells from moving to areas of the body such as in the kidney where they cause abnormal scarring. Dimerix identified that the CCR2 receptor and the angiotensin II receptor type 1 (AT1R) are G Protein Coupled-Receptors (GPCRs). GPCRs in general are signalling molecules that pass the signals onto intracellular 'G proteins'. They are present in just about every organ system, and as a result have been considered as targets for a wide range of disease areas including heart disease, cancer, diabetes, inflammation, and CNS disorders. AT1R forms a GPCR heteromer with CCR2, therefore demonstrates a synergistic benefit when blocking both receptors at the same time, and this is highly relevant in the kidney.

FSGS

The progressive nature of kidney diseases results in poor prognosis for patients, thereby culminating in total kidney failure and a poor quality of life. When the kidneys fail, they are likely to stop working well for the patient to survive without dialysis or a kidney transplant. The cost of a kidney transplant in Australia is A$260,000 per patient with ongoing and expensive anti-rejection drugs costing thousands of dollars per year, and dialysis costs in the range of A$100,000 per patient per year. The dialysis also requires regular visits, to a total of over 12 hours per week to the medical facility. This serves as a huge burden on both the patient and the healthcare system.

FSGS is a specific kidney disease attacking the kidney's filtering units, thereby resulting in irreversible scarring and permanent kidney damage.

FSGS is a one of the most common forms of acquired glomerular diseases leading to end stage kidney disease (ESKD). It is a specific kidney disease that attacks the kidney's filtering units where the blood is cleaned (called the glomeruli). This causes irreversible scarring and leads to permanent kidney damage and eventual end-stage kidney failure, requiring dialysis or a replacement. The average time from a diagnosis of FSGS to the onset of complete kidney failure is only five years and it affects both adults and children as young as two years old. Approximately 60% of those who receive a kidney transplant risk will get re-occurring FSGS in the transplanted kidney. Thus, a high unmet need exists for FSGS as it is a disease that can impact both adults and children and can be caused by a variety of conditions. There are no drugs specifically approved for FSGS anywhere in the world. Any drugs that are used target symptoms rather than the disease itself.

Dimerix's clinical endeavours with DMX-200

Dimerix ran two Phase 2 studies between 2018 and 2020, giving them the code name 'ACTION', short for ' AT1R and CCR2 Targets for Inflammatory Nephrosis'. ACTION for FSGS was a small Phase 2a study of 10 patients while ACTION for DKD was a 40-patient Phase 2b. Both studies were 'cross-over' studies conducted in Australia, meaning every patient received both drug and placebo at some point during the study. In March 2020, after these studies had completed recruitment, Dimerix announced that some patients had stayed on the drug (including some from the 2017 study) via a 'Special Access Scheme' authorised by Australia's Therapeutic Goods Administration. Data from ACTION Phase 2a for FSGS and ACTION Phase 2 for DKD read out in July 2020 and September 2020 respectively.

Dimerix developed a new formulation for DMX-200. Prior to the Phase 2a study in FSGS, the company took the active ingredient, repagermanium, and created a revised, commercially viable formulation that only needed to be taken twice daily rather than three times daily as in earlier studies[1]. The company further revised the formulation to ensure manufacturing ease. Not only was the revised formulation more convenient for the patients, but the reformulation was also scalable meaning it was now suitable for large scale commercial manufacturing. Under the relevant laws covering new drugs, known as a New Chemical Entity, for an orphan disease, such as DMX-200 can attract seven years exclusivity in the US and 10 years in the EU regardless of patent protection which can be extended by a further 2 years in Europe and 6 months in US for a paediatric indication. In addition, Dimerix also has been granted patent protection in key territories until at least 2032 (method of use) and further patent applications in that could extend that to 2042 if granted (formulation and method of use). The relevant patent application was published in 2023.

The bottom line is that Dimerix entered a Phase 3 trial for FSGS as the indication because Orphan Drug designation (ODD) meant a single and more manageable Phase 3 clinical study with the potential for accelerated approval in a disease with no approved treatments. The Diabetic Kidney Disease trial found that DMX-200 was safe and well-tolerated. Furthermore, the drug was effective in reducing proteinuria and albuminuria, although, at 12 weeks the trial did not show the treatment was statistically better than the placebo, seeing a strong placebo response in the short study. While investors were disappointed with the initial results in diabetic kidney disease, the subsequent assessments of the data depicted all hope was not lost. A greater effect was

[1] See the Dimerix market release dated 8 January 2018 and headlined DMX-200 dosage optimisation study successfully completed in preparation for Phase 2b trial.

seen in patients after the completion of the trial, leading the company to believe that that a longer study treatment duration was warranted and would have likely demonstrated better results. Dimerix may revisit Diabetic Kidney Disease after the FSGS indication is live.

The ACTION3 trial (2022)

Dimerix is now in Phase 3 with DMX-200 for FSGS. As per 2021 guidance, Dimerix only needs a single Phase 3 study of DMX-200 to gain approval in both the US and the EU, and potentially in China too.

There are two basic endpoints for the Phase 3 study: uPCR and eGFR:

- **uPCR is urinary Protein to Creatinine Ratio**, the standard way of measuring proteinuria. When kidneys are damaged, protein can leak into the urine, causing proteinuria, hence proteinuria can represent an important early marker of kidney function. uPCR is kidney protein concentration in milligrams in a patient's urine, divided by the creatinine concentration in grams. Creatinine is a breakdown product of creatine phosphate from muscle which is routinely excreted through the kidneys and provides a good reference to how hydrated a patient is.

- **eGFR is estimated Glomerular Filtration Rate**, the flow rate of filtered fluid through the kidney in millilitres per minute. Specifically, it is millilitres per minute per 1.73m^2, the latter figure being the average body surface area for an adult. GFR can't be measured directly so is estimated (the 'e' in eGFR) by testing for the blood levels of creatinine, which, we noted above, is normally cleared from the blood by the kidneys. When kidney function is declining the level of creatinine in the blood goes up. A normal GFR in a young adult is greater than 90 mL/min/1.73m^2.

Encouraging interim analysis results for the ACTION3 Phase 3 trial

Passing the first interim analysis is a key milestone for Dimerix. It has paved the way to move ahead with the second interim analysis

The ACTION3 Phase 3 trial of DMX-200 in patients with FSGS was successful in the first interim analysis based on the proteinuria efficacy endpoint of the study. ***The trial was conducted on 72 random patients and indicated that DMX-200 is performing better than placebo in terms of reducing proteinuria in a much larger cohort than the prior Phase 2 study*** (comprising of eight patients).

An interim analysis comprising a futility assessment[2] was conducted to gauge whether the trial has efficacy and whether it will meet its objective if completed. The successful interim analysis outcome is a key milestone for the company and suggests that DMX-200 may result in improvement in kidney function when included to the standard of care in patients with FSGS.

Post notifying the company of the interim analysis results, the trial's Independent Data Monitoring Committee (IDMC) also stated that it had no safety concerns related to DMX-200. IDMC also recommended that the ACTION3 clinical trial to continue as planned. This, in turn, further validates the strong safety profile of DMX-200.

[2] In a futility assessment data is assessed early to see whether a drug is having desired effect or not.

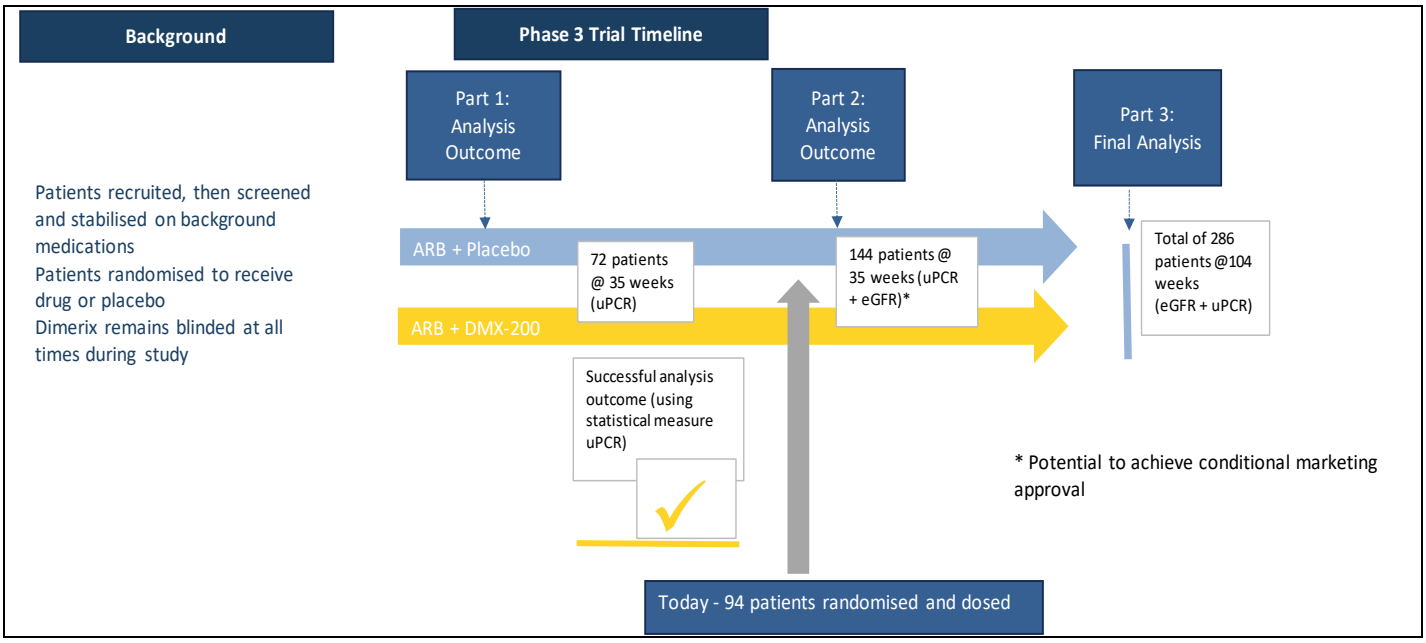
Figure 1: Current (in green) and planned (in black) recruitment site locations for Phase 3 trial

Source: Company

The ongoing Phase 3 trial is currently being conducted at over 70 clinical sites in 11 countries including Australia, New Zealand, Taiwan, Hong Kong, France, Denmark, the UK, Spain, Argentina, Brazil, and the US. New clinical sites have also been planned at China, Malaysia, Italy, Germany, Portugal, and Mexico to further enhance the recruitment process (Figure 1).

The positive results from the Phase 3 Part 1 trial have paved the way to move ahead with Part 2 of the study. The Part 2 will have approximately 144 patients enrolled for 35 weeks' treatment and will include children up to 12 years old as well as adults (Figure 2).

Figure 2: ACTION3 Phase 3 clinical trial – next steps



Source: Company, Pitt Street Research

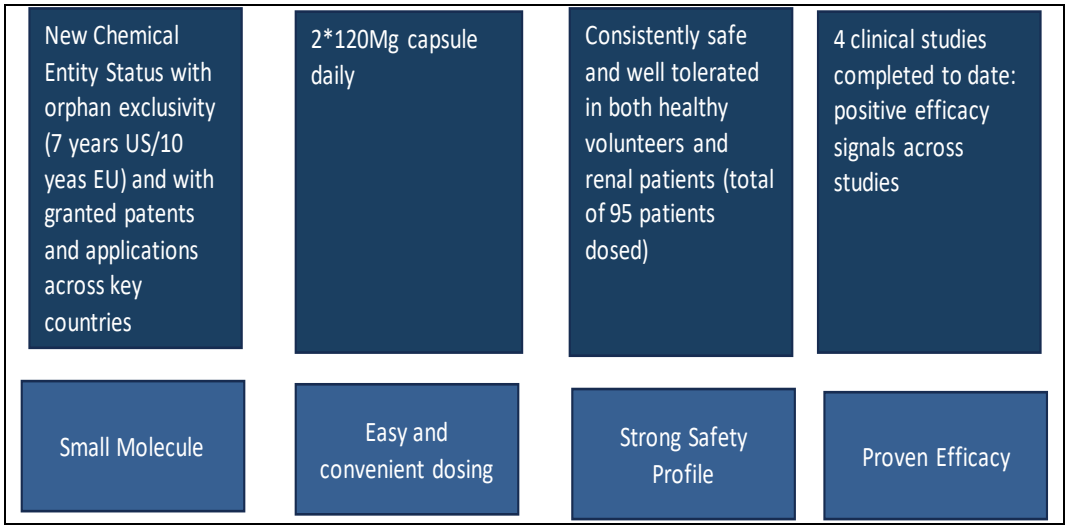
The outcome of the second interim analysis is expected by mid-CY25.

The outcome of the second interim analysis is expected by mid-CY25 and will be very crucial as it is designed to capture evidence of proteinuria and kidney function (eGFR slope), which is expected to generate sufficient evidence to support conditional marketing approval. **In our view, this will significantly boost the company's growth prospects, as Dimerix will gain early market access in select geographies.**

DMX-200 is working on an inflammatory signalling pathway

DMX-200 is working on an inflammatory signalling pathway. The pathway being targeted is composed of small molecules, easy and convenient dosing, strong safety profile and proven efficacy (Figure 3).

Figure 3: Inflammatory signalling pathways



Source: Company, Pitt Street Research

Dimerix has set clear milestones for the near term

Dimerix has laid down some key milestones. These include product development and commercialisation under which Dimerix aims to complete Phase 3 clinical trial in FSGS, including clinical, non-clinical manufacturing, IP, quality, and regulatory fields. The company also aims to attract additional partners to realise inherent value in existing assets and provide early revenue and risk management to the company through upfront and milestone payments and royalties. Another key milestone includes expansion of the product portfolio, achieving strong valuation of the company given a valuable product portfolio and commercialisation and expansion of the talent pool. Some other key milestones include interim analysis expected from the Phase 3 clinical trial, execution of potential licensing deals for jurisdictions including the US and China, recruitment and dosing of 144 patients for Part 2 (with the second analysis outcome estimated around mid-2025) as well as announcements pertaining to the company's secondary assets.

Strategic partnerships in nephrology bode well for growth prospects

Dimerix has received significant partnership interest from pharmaceutical companies globally. The company's preference is to work with experienced and capable partners. The partners are likely to be ones with regulatory, sales and marketing infrastructure with experience in the desired territories. Dimerix has received non-binding term sheets for regional deals, with multiple parties in the data room conducting due diligence and negotiating a potential licensing agreement for several territories.

Currently, Dimerix is in a partnership with Advanz Pharma. The former is likely to receive up to A$230m in upfront and milestone payments plus royalties. These include A$10.8m received in November 2023, A$218m in potential development and sales milestones and tiered royalties on net sales.

Partnerships are likely to be available for multi-billion dollar markets including the Us and China.

We believe that partnerships are likely to be available for potential multi-billion dollar markets, including the US and China. In particular, China represents a large market with the recent licensing transaction representing a potential upside.

Capital raising initiatives to solidify financial position

Almost immediately after the first interim results, Dimerix raised A$20m at an issue price of A$0.30 via an institutional placement. Proceeds from the placement are likely to be utilised to complete the ACTION3 Phase 3 clinical study in patients with FSGS, preparation and submission of regulatory applications as and when applicable to continue the FSGS Phase 3 clinical study, continued manufacturing distribution and logistics of the required clinical trial material, partnership activities as well as working capital and offer costs.

The placement should provide sufficient funds to take Dimerix through the second interim analysis and the completion of the ACTION3 Phase 3 Clinical trial, including eligible R&D rebates.

We update our valuation to A$0.63 per share in our base case and A$0.83 per share in our bull case.

Our valuation of Dimerix

In our initiation report prepared in January 2024, we had valued Dimerix using the Discounted Cash Flow (DCF) approach. Our total valuation was A$0.58 per share under the base case projection, while our bull case projection placed the valuation at A$0.77 per share equating to equity values of A$246.3m and A$326.3m, respectively. In light of the company's results and its recent capital raising, we update our range. We have reduced the discount rate to 12.2% by reducing the beta from 1.5x to 1.1x but kept our go-to-market assumptions - namely regulatory approval, pathway to market, milestone revenue, and market size and penetration - unchanged. Our new equity value is $346.7m in our base case and $456.8m in our bull case. This would equate to $0.81 per share and $1.07 respectively under 426.1m shares on issue, although the company's shares on issue now stands at 547.2m following the recent capital raising. Our base case scenario is therefore $0.64 per share in our base case and $0.84 in our bull case (Figure 4).

Figure 4: DXB's DCF calculation

Valuation (A$m)	Base Case	Bull case
Present Value of FCF	139.0	181.5
Present Value of Terminal Value	201.1	268.7
Enterprise Value (A$ m)	**340.1**	**450.2**
Net (debt) cash	(6.6)	(6.6)
Minority Interest	-	-
Other Investments	-	-
Equity value (A$ m)	**346.7**	**456.8**
Shares outstanding	547.2	547.2
Implied price (A$ cents)	**0.63**	**0.83**
Current price (A$ cents)	0.30	0.30
Upside (%)	112.0%	178.3%

Estimates: Pitt Street Research

Catalysts for DXB's re-rating

We see the key clinical catalyst as being the next set of successful interim data being read out as being the key catalyst for the stock. The company has told investors this would be 35 weeks after the 144th patient had been recruited, and based on current recruitment timelines is expected around mid-CY25. Thereafter, we expect momentum as the company eventually applies for regulatory approval. Dimerix's efforts with FSGS aside, we think there is also potential for upside from success with its endeavours against Diabetic Kidney Disease, although these are on hiatus for now.

It is also plausible that future partnerships could be a key catalyst for the creation of shareholder value. The EU market, covered by the current Advanz deal is worth $230m and only 20% of the global opportunity.

Our initiation report declared that DXB was a Phase 3 stock priced like a Phase 2 stock. Notwithstanding DXB's re-rating since the ACTION3 initial analysis, we still think this point is true in light of Phase 3 biotechs trading at higher enterprise values such as Opthea (ASX:OPT). At the same time, we think the results are an important step towards closing the gap between DXB and other Phase 3 biotechs.

Key risks facing Dimerix

Risks specific to DXB - We see the following major risks for DXB as a company and as a listed stock:

- Timing risk. There is the risk that the company's products may take longer than expected to move through the clinic, especially with clear time frames that are imminent – in particular, clinical data by mid-March.

- Regulatory risk. There is the risk that regulators may decline to approve DXB products, even if DXB considers the data submitted to be adequate.

- Commercial risk. There is the risk that DXB may fail to find more commercial partners for its products. We note it has been de-risked for some jurisdictions, although there is also the risk for commercial partnerships to fall apart.

- Uptake risk. There is the risk that DXB products are still too expensive in the healthcare markets in which it wants to participate.

- Funding risk. There is the risk of future capital raisings proving dilutive to existing shareholders.

- Key personnel risk. There is the risk that the company may lose key personnel and be unable to replace them and/or their contribution to the business.

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 stocks exchanges in Australia and around the world 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 the stock of any biotechnology and medical device stock mentioned in this report, including Dimerix.

Appendix I - Analyst certification

Stuart Roberts, lead analyst on this report, has been an equities 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 speciality 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 over 2015–2016 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 Sciences 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 Sciences companies.
- Since 2018, Stuart has led Pitt Street Research's Resources Sector franchise, spearheading research on both mining and energy companies.

Nick Sundich, lead analyst on this report, is an equities research analyst at Pitt Street Research.

- Nick obtained a Bachelor of Commerce/Bachelor of Arts from the University of Sydney in 2018. He has also completed the CFA Investment Foundations program.
- He joined Pitt Street Research in January 2022. Previously he worked for over three years as a financial journalist at Stockhead.
- While at university, he worked for a handful of corporate advisory firms.

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