PITT STREET RESEARCH

Prescient Therapeutics

New T-Cell Lymphoma therapy coming soon

Share Price: $0.056

Prescient Therapeutics is a Melbourne-based drug developer focused on cancer, with several platforms and products in its portfolio. Prescient Therapeutics' lead compound is a small molecule called PTX-100, which is potentially a significant future treatment for T-Cell Lymphoma. The company also has two cell therapy platform technologies: OmniCAR, which allows next-generation CAR-T (Chimeric Antigen Receptor T-cell therapy) products to be developed, and CellPryme, which allows enhances adoptive cell therapy performance.

ASX: PTX

Sector: Healthcare

9 November 2023

Market Cap. (A$ m)	45.1
# shares outstanding (m)	805.3
# shares fully diluted (m)	837.2
Market Cap Ful. Dil. (A$ m)	46.9
Free Float	100%
52-week high/low (C$)	0.185 / 0.053
Avg. 12M daily volume ('1000)	645.9
Website	https://ptxtherapeutics.com

Source: Company, Pitt Street Research

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

Source: Refinitiv Eikon, Pitt Street Research

A big payday coming soon with PTX-100

PTX-100, which works as a blocker of the GGTase I enzyme, has Orphan Drug Designation for all T-Cell Lymphomas and is currently in a Phase 1 trial. There is potential for this product to gain FDA approval after Phase 2 given the current lack of treatment options for T-Cell Lymphomas.

CellPryme and OmniCAR are improvements on existing CAR-T technologies

CAR-T has emerged in recent years to be an important part of the cancer world, ever since the successful commercialisation of Kymriah from Novartis and Yescarta from Gilead. CellPryme, with its improvements on existing technologies, potentially represents a way to produce cellular immunotherapies that can overcome a suppressive tumour microenvironment. The CellPryme platforms have the potential to deliver quickly for Prescient given their ability to improve existing cellular therapies. PTX's OmniCAR platform enables controllable T-cell activity and multiantigen targeting with a single cell product. Normally with CAR-T a single cell targets a single antigen, and the T-cell activity, once it is unleashed, is not controllable. OmniCAR allows solutions to both these problems to be created.

Valuation metrics	
DCF fair valuation range (A$c)	11.6-16.3
WACC	16.2%
Assumed terminal growth rate	None

Source: Pitt Street Research

Valuation range of 11.6-16.3c per share

We value PTX at 11.6c per share base case and 16.3c per share in an optimistic (or bull) case using a Sum of the Parts/DCF methodology. Please see p.19 for an outline of our valuation rationale and p.21 for the key risks.

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Introducing Prescient Therapeutics

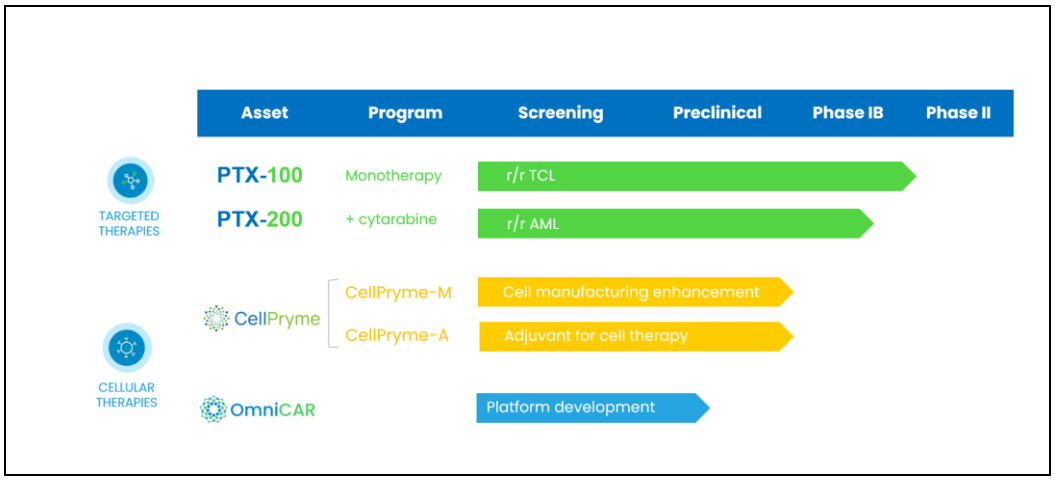
Prescient Therapeutics is a biotech company with the OmniCAR and Cell Pryme technologies.

Prescient Therapeutics (ASX: PTX) is a biotech company specialising in oncology. It has two novel small molecule therapeutics - PTX-100 and PTX-200 - as well as the OmniCAR and CellPryme technologies (Figure 1). OmniCAR allows next-generation CAR-T products to developed, while CellPryme allows enhances adoptive cell therapy performance. PTX-200 is now non-core for Prescient while PTX-100 is the company's lead molecule, with potential to deliver strong shareholder value in the near term because of demonstrated clinical utility in T-Cell Lymphoma.

PTX originated with PTX-100 and PTX-200 in 2014. The Australian bio-entrepreneur Paul Hopper licensed the rights to PTX-100, then called GGI-2418, from Yale University. This project was vended in a reverse shell transaction, using the shell of a failed drug developer called Virax. This deal was completed in May 2014. The acquisition of PTX-200 was announced in October 2014 and completed in December 2014, at which point the name Prescient Therapeutics was adopted.

Prescient publicly entered the cell therapy space with OmniCAR in May 2020, in-licensing the two parts of the OmniCAR platform from the University of Pennsylvania and Oxford University. CellPryme, on which Prescient was working prior to the OmniCAR announcement, was, technically speaking, the company's first foray into cell therapy, where it sought to leverage its biochemistry and immunology experience. That platform emerged from 'stealth mode' in 2022. CellPryme is a platform technology developed internally by Prescient designed to do produces superior cells during the cell manufacturing process. The original CellPryme-M platform, announced in June 2022, was designed to produce better cells for CAR-T. CellPryme-A, announced in September 2022, is an adjuvant therapy designed to be administered to patients alongside cellular immunotherapy to help them overcome a suppressive tumour microenvironment.

Figure 1: PTX's pipeline



Source: Company

PTX-100

PTX-100 is PTX's lead compound and has potential to be a future treatment for T-Cell Lymphoma. PTX-100 is small molecule that can attack cancer by disrupting a cellular signalling pathway called 'Ras'. This drug is now in a Phase 1b expansion cohort study in T-Cell Lymphomas, where it is showing encouraging efficacy and

safety. In March 2023 the US FDA has granted PTX-100 Orphan Drug Designation for all T-Cell Lymphomas. Since T-Cell Lymphoma is a disease condition with no adequate treatments at present, there is potential for the FDA to clear PTX-100 after Phase 2 if the data is good.

CellPryme also represents a major opportunity

CellPryme is another technology platform held by PTX consisting of two complementary CellPryme applications, CellPryme-M and CellPryme-A. The idea behind it is that the addition of certain genetic material during the production of cellular medicines improves the performance of the medicine.

CellPryme-M is designed to improve the performance of whatever CAR-T cell therapy employs it by making more 'youthful' cells, that live longer and kill cancer cells for longer. It does so by shifting T and NK cells towards a central memory phenotype, improving persistence, and increasing the ability to find and penetrate tumours. CellPryme-A is designed to produce superior cellular immunotherapies that can dramatically increase proliferation of CAR-T cells in vivo; overcome a suppressive tumour microenvironment and increase CAR-T penetration into tumours.

OmniCAR is an improvement on existing CAR-T technologies

CAR-T cell therapy is a novel scientific approach that utilises the body's own immune system to fight cancer.

CAR-T cell therapy is a therapeutic approach that utilises the body's own immune system to fight cancer (specifically the T-cells). It works by extracting T-cells from the patient's blood and then genetically engineering them to produce 'Chimeric Antigen Receptors' on their surface which directs a T-cell response to that specific cancer antigen. Subsequently, the patient receives the CAR-T cell therapy in an infusion that can target and destroy cancer cells.

CAR-T has emerged in recent years to be an important part of cancer treatment. The world's first CAR-T therapy, Kymriah from Novartis, gained FDA approval in 2017 and by 2022 had reached sales of more than US$1bn. While the clinical results have been positive, there are some shortcomings including high costs and lack of control post-administration. PTX's therapies have the potential to overcome some of these problems.

OmniCAR is a universal immune receptor platform and a molecular binding system. It was in-licensed by Prescient in 2020 from the University of Pennsylvania and Oxford University. OmniCAR enables controllable T-cell activity and multiantigen targeting with a single cell product and thereby leads to stronger treatment outcomes when used in CAR-T therapy, overcoming the two problems mentioned above, among other benefits. PTX's preclinical work with OmniCAR has delivered impressive results and the company plans to bring it into the clinic in due course.

Importantly, PTX's platform is useful not just in CAR-T but in other adoptive cell therapies such as CAR-NK, and so on.

A big 12 months ahead

We see Prescient Therapeutics re-rating as PTX-100 nears the end of Phase 2

PTX is only capitalised at A$45m despite having $21.3m cash and compelling clinical candidates. The bear market for Life Sciences since late 2021 has knocked down the value of all kinds of biotech and medical device companies on all exchanges globally – including many comparable companies to PTX. But we see Prescient Therapeutics re-rating as PTX-100 nears the end of Phase 2, and as the first product candidates emerge from the Cell Pryme platforms.

A payday is coming soon for Prescient thanks to T-Cell Lymphoma

Currently Prescient stock is seriously undervaluing a potential near-term payday with PTX-100. Prescient Therapeutics had a market capitalisation on ASX of less than $50m, which is only US$32m. Whatever currency you use, we think the current market capitalisation of Prescient does not begin to take account of the way in which clinical success with PTX-100 in T-Cell Lymphoma can yield a marketed drug in only around three years, where that drug's market opportunity is at least in the hundreds of millions.

Over the last four years Prescient has gathered some great data on PTX-100 in T-Cell Lymphomas. The drug had been in Prescient's portfolio since it acquired the rights in 2014. In 2019 Prescient started a Phase 1 study of PTX-100, initially as a dose escalation study in a variety of tumour types. Phase 1b completed in July 2021 with an excellent safety profile and a clinical signal in T-Cell Lymphoma. This was the clue Prescient needed in terms of how to take PTX-100 forward. An expansion cohort in T-Cell Lymphoma opened in April 2022 to focus on T-Cell Lymphomas and by October 2022 Prescient was reporting favourable clinical activity in this cohort. In July 2022 PTX-100 was granted Orphan Drug Designation by the US FDA in July 2022 for Peripheral T-Cell Lymphoma and for all T-Cell Lymphomas in March 2023. By that time seven of 10 patients T-Cell Lymphoma patients evaluated had durations of response exceeding the standard of care.

In just three years from now, Prescient can be close to having PTX-100 as a marketed drug

In just three years from now, Prescient can be close to having PTX-100 as a marketed drug. That's because the data to date shows that PTX-100 markedly exceeds the standard of care, in cancer indications where that standard of care is less than optimal. Consequently, we expect that, once the current Phase 1 is completed, only a single Phase 2 might be required by the FDA. Should that study yield sufficiently good data, the Agency may be prepared to grant the drug marketing authorisation. That could happen in only around three years' time, with the Phase 2 potentially initiating in late 2024 and reading out data in late 2026. Even if the FDA decides that this Phase 2 is not a registration trial, having a drug as powerful as PTX-100 seems to be in Phase 2 will still warrant a re-rate, given the responses noted in Phase 1.

Orphan Drugs can be very valuable, for their developers. In the US an 'Orphan Drug' is one that treats a disease affecting fewer than 200,000 Americans. In addition to tax credits, Congress incentivised pharmaceutical companies through the Orphan Drug Act of 1983 with a waiver of prescription drug user fees and by offering seven years of market exclusivity after the drug is approved, rather than the standard five years. In more recent years, Orphan Drugs have become notable not so much for these incentives as the high prices they can sell for. A good example is Soliris and Ultomiris, from AstraZeneca, each of which has a US$650,000-a-year price tag to treat two obscure blood disorders. They made close to $6bn for AstraZeneca in 2022. Because of the high prices, Orphan Drug developers on Nasdaq will often trade for large market capitalisations once they have products on the market. Consider Amgen’s buyout of Horizon Therapeutics in October 2023. Amgen bought Horizon for Tepezza, which is the only approved treatment for thyroid eye disease. Horizon earned $1.66bn in sales for Tepezza in 2021, in its first full year on the market, and US$1.97bn in 2022. Amgen paid a massive US$27.8bn for this new franchise.

Prescient has the goods with PTX-100. Since 2021 there has been growing evidence that the data that PTX-100 is highly effective in T-Cell Lymphoma:

- **July 2021**. One patient in the Phase 1b with peripheral T cell lymphoma (PTCL) had failed five prior treatments. For that patient PTX-100

generated a partial response and no disease progression for the next 17 months. Another patient with cutaneous T cell lymphoma (CTCL) had failed three prior treatments and stayed on drug for another 12 months. This beat the usual standard of care where there would have been disease progression within four months.

- **October 2022**. By October 2022 four patients in the expansion cohort who had PTCL and three with CTCL had been dosed. A PTCL patient registered a partial response despite failing five previous lines, with that response lasting 32 months before progression. Another had a ' very good partial response' after failing four lines.
- **March 2023**. By March 2023 there were eight PTCL and five CTCL patients dosed. Of ten evaluable patients the Overall Response Rate was 40% and the Progression Free Survival was an average of 8.7 months. This was good because when Seagen's Adcetris drug had been studied in Phase 3 in CTCL, the PFS benchmark that it had to beat was a median of four months, this being 'physician's choice' of either methotrexate or bexarotene[1].

What is the catalyst for PTX-100-driven re-rating? Guidance from the FDA as to what clinical data it will require, which Prescient will seek in early 2024, has the potential to start a re-rating given what we know about PTX-100 in T-Cell Lymphoma.

[1] Horwitz et. al. (2021), *Randomized phase 3 ALCANZA study of brentuximab vedotin vs physician's choice* in cutaneous T-Cell Lymphoma: final data. Blood Adv. 2021 Dec 14;5(23):5098-5106.

Ten reasons to look at PTX

1. **Prescient may have the Next Big Thing in T-Cell Lymphoma** with PTX-100. The Phase 1b data on Prescient's PTX-100 drug is favourable in T-Cell Lymphomas. Since T-Cell Lymphoma is a disease condition with no adequate treatments at present, there is potential for the FDA to clear PTX-100 after Phase 2 if the data is good. PTX could well be the only ASX small cap biotech with a cancer drug in a pivotal clinical trial.
2. **The market opportunity in T-Cell Lymphoma is lucrative**. While only around 5,000-6,000 people a year will be diagnosed with a T-Cell Lymphoma in the US the market opportunity could be in the billions, if Acrotech Biopharma's Folotyn with its $842,585per patient per year price tag is any guide.
3. **Prescient is an Orphan Drug developer**, with PTX-100 having Orphan Drug status in the US for all T-Cell Lymphomas since March 2023. Orphan Drug status brings certain benefits such as seven years of market exclusivity and other benefits such as tax credits, fee waivers, and access to specialized regulatory assistance.
4. **PTX-100 has multiple future indications**. Given the role the GGTase I enzyme plays in the pathways related to Ras, there is potential for PTX's drug to work against myeloma, breast cancer and pancreatic cancer.
5. **Prescient has significant R&D capabilities in-house**. The CellPryme technologies, that improve the quality of cellular medicines, was largely developed by Prescient's own team in-house. This capability bodes well for future product development.
6. **CellPryme can markedly improve the quality of all kinds of cellular therapies**. The ability of CellPryme to make the cells in cellular therapies more 'youthful' (CellPryme-M), as well as overcome a suppressive tumour microenvironment (CellPryme-A), allows a relatively rapid path to commercialisation given the many cellular therapy products now in the clinic.

Prescient's OmniCAR platform can potentially take the CAR-T field to the next level.

7. **Prescient's OmniCAR platform allows next generation CAR-T**. Conventional CAR-T has been highly successful, both clinically and commercially, but Prescient's OmniCAR platform, by allowing controllable T-cell activity and multiantigen targeting with a single cell product, can potentially take the CAR-T field to the next level.
8. **The success of CAR-T since 2014 suggests many potential partnering deals for Prescient with both CellPryme and OmniCAR**. The world's first CAR-T therapy, Kymriah from Novartis, gained FDA approval in 2017 and by 2022 had reached sales of more than US$1bn.
9. **Prescient has a quality leadership team**. CEO Steve Yatomi-Clarke has grown Prescient from near start-up in 2016 to a company with a solid pipeline of clinical products and two credible platforms in OmniCAR and CellPryme. His success in securing OmniCAR from the University of Pennsylvania was particularly creditable. Backing Steve is a solid board chaired by the American biotech veteran Steve Engle.
10. **Prescient is undervalued on our numbers**. We value Prescient at 11.6 cents in our base case and 16.3 cents in our optimistic case. We see Prescient re-rating as it continues to generate good clinical data from assets in the pipeline and move towards eventual commercialisation. We also see upside potential as products from the OmniCAR platform moves towards being studied in clinical trials.

PTX-100

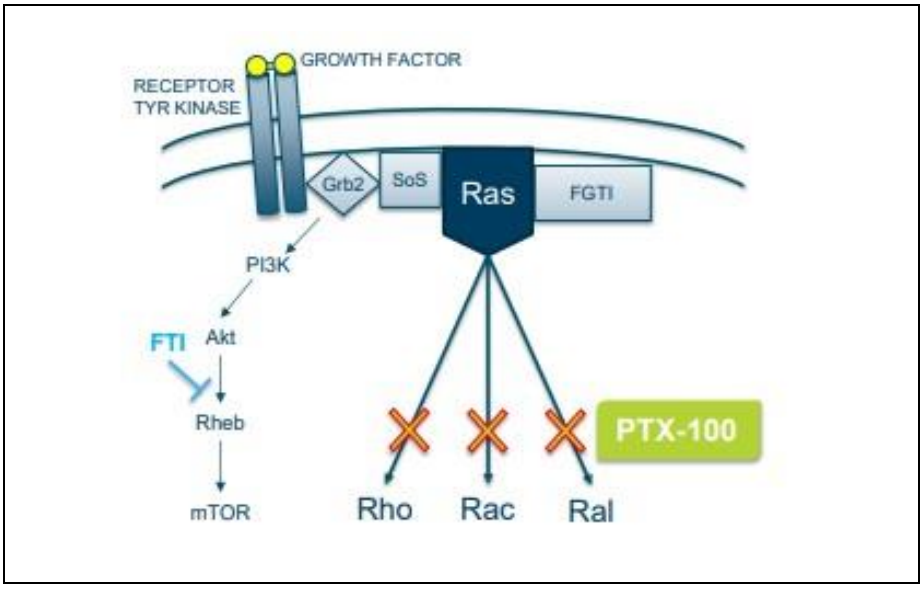
PTX-100 potentially represents a new treatment for T-Cell Lymphoma.

PTX-100 is one of two drugs PTX has in the clinic, targeting T-Cell Lymphoma. This drug, administered intravenously, was picked up by PTX in 2014 and was granted Orphan Drug Designation by the US FDA in July 2022 for Peripheral T-Cell Lymphoma and for all T-Cell Lymphomas in March 2023.

The history of PTX-100

PTX-100 was invented around 2009 by Professor Said Sebti who was then at the H. Lee Moffitt Cancer Center in Tampa, Fl., and Professor Andrew Hamilton[2], who had then recently completed his time as Provost of Yale University[3]. The pair were exploring the potential of inhibitors of an enzyme called Geranylgeranyl transferase I (GGTAse I) and PTX-100, a peptidomimetic small molecule inhibitor of GGTase I. PTX-100 was specifically designed to block this enzyme. By the time PTX-100 came to Prescient in 2014 the drug had been tried out in a small Phase I in 13 patients with multiple tumour types, where four patients had registered stable disease[4]. Sebti was interested in the potential of the treatment in myeloma, breast cancer and pancreatic cancer among other cancers.

Figure 2: How PTX-100 operates



Source: Company

Prescient started a Phase 1 study of PTX-100 in 2019, initially as a dose escalation study in a variety of tumour types. The lead investigator was Professor Miles Prince at the Epworth Clinic in Melbourne. The study dosed its first patients in November 2019 and was successfully escalated to 2,000 mg/m^2. The study completed in July 2021 with an excellent safety profile and a clinical signal seen in T-Cell Lymphoma. Ever since, PTX-100 has been focused on T-Cell Lymphoma.

[2] Hamilton was Provost of Yale University from 2004 to 2008 and then Vice Chancellor of the University of Oxford from 2009 to 2015. He was President of New York University from 2016 to 2023.
[3] See *Methods for inducing tumor regression, inhibiting tumor growth, and inducing apoptosis in breast tumors with Geranylgeranyltransferase I inhibitors*, WO/2010/088457, priority date 29 January 2009.
[4] See Karasic et. al., Target Oncol. 2019 Oct;14(5):613-618.

PTX-100 works by blocking the GGTase I enzyme.

How PTX-100 works

PTX-100 works by blocking the GGTase I enzyme. A lot of cancer drugs work by disrupting aberrant cellular signalling pathways that are preventing the cell from undergoing apoptosis, that is, normal cell death. GGTase I is an enzyme that acts on a protein called Rho and that protein in turn is part of the large Ras superfamily of pathways (Figure 7). Ras mutates in 30% of all human cancers and up to 90% in some specific cancers. The potential power of blocking GGTase I is that multiple pathways, including Rho, Rac, and Ral, within the Ras superfamily are impacted, prompting the cancer cell to undergoing apoptosis.

PTX-100 has had strong responses in relapsed and refractory T-Cell Lymphoma

PTX-100 development has been focused on T-Cell Lymphoma since 2021. The clinical signals PTX obtained from PTX-100 in 2021 led to an expansion cohort in April 2022 to focus on this cancer. Prescient reported favourable clinical activity in this expansion cohort in October 2022. By March 2023 40% of patients had responded, and seven of 10 patients evaluated had durations of response exceeding the standard of care. What was important was this expansion cohort represented relapsed and refractory patients.

The T-Cell Lymphomas represent an area of unmet medical need. There are numerous subtypes of T-Cell Lymphoma, including Angioimmunoblastic T-Cell Lymphoma, T-cell Lymphoblastic Lymphoma, Cutaneous T-Cell Lymphoma (CTCL), Anaplastic Large Cell Lymphoma (ALCL) and Peripheral T-Cell Lymphoma. What all these subtypes have in common is that there has been a death of new drugs in recent years. Generally overall survival in relapsed or refractory disease is less than a year in the absence of an allogeneic hematopoietic stem cell transplantation, which can be expensive[5].

There is potential to gain FDA approval after Phase 2. If an experimental therapy is particularly strong compared to the standard of care there is potential for it to gain FDA approval after Phase 2, at the Agency's discretion. Given the lack of treatment options in relapsed and refractory T-Cell Lymphoma, Prescient believes post Phase 2 approval is a serious possibility for PTX-100.

[5] Cancers (Basel). 2023 Feb; 15(3): 589. Published online 2023 Jan 18.

Estimating a market size for PTX-100

Estimating a market size for PTX-100 is difficult, because, as we noted above, there are multiple subtypes of T-Cell Lymphoma and little consensus among oncology professionals as to the gold standard[6]. And that's before you even consider that many drugs approved against a T-Cell Lymphoma are only approved against a certain type (such as peripheral, angioimmunoblastic, anaplastic, intestinal and extranodal).

There are four agents for the treatment of Relapsed Peripheral T-Cell Lymphoma to have received FDA approval in the last decade: Pralatrexate, Romidepsin, Belinostat and Brentuximab Vedotin. Romidepsin was taken off the market following the FDA's withdrawal of approval for peripheral T-Cell Lymphoma. For Brentuximab Vedotin, or Adcetris (an antibody-drug conjugate belonging to Seagen Inc, Nasdaq SGEN), data is available. Adcetris has also become the first FDA drug for newly diagnosed T-Cell Lymphoma. It recorded US$839m in sales during CY22, up 19% from CY21's total. Based on sales during the first 6 months of CY23, it is on track to surpass US$1bn in sales for the full calendar year. Adcetris is used for other indications too including classical Hodgkin lymphoma and relapsed systemic anaplastic large call lymphoma[7] so it would be a vague syllogism to conclude the market size is US$1bn. That said, US$1bn is not unreasonable for a drug with PTX-100's potential versatility.

The best analogy for PTX-100 is Pralatrexate/Folotyn), a US$2.4bn opportunity in the US alone. Folotyn, generic name pralatrexate, was first FDA approved in 2009 and has remained on the market but only against Relapsed or Refractory Peripheral T-Cell Lymphoma. Fierce Pharma recently suggested that Folotyn cost in the order of US$840,000 per year in the US, making it that country's 10th-most expensive drug in 2023[8]. This for a drug with a response rate of less than 30%![9]. Using an earlier estimate from PTX of US$450,000 and assuming 5,500 patients per annum (a midway point between 5-6,000 patients which are estimated to be the numbers of people in the US diagnosed with T-Cell Lymphoma[10], we estimate a total revenue opportunity of ~$2.4bn. The rest-of-world opportunity could potentially expand this to US$5bn[11]. We acknowledge the market opportunity could be smaller if PTX-100 is only approved against Peripheral T-Cell Lymphoma – and this could well be the case given this was the scope of its recent clinical efforts to date. However, we believe this is an adequate starting point to estimate the total market opportunity. And it is possible PTX-100 could be approved against all T-Cell Lymphomas given the company has a separate Orphan Drug designation for all T-Cell Lymphomas having already obtained one for Peripheral.

The market opportunity could be even greater than US$2.4bn when you consider it could eliminate costs to the health system currently caused by existing treatments. One example is medical treatments that may be required from side effects - Folotyn comes with a greater than 75% chance of serious side effects but PTX-100 has reported no serious adverse effects to date. We noted above that CAR-T therapy tends to be US$1-$1.5m when all costs are considered. This could mean the total market opportunity could be US$5-$9bn. It's also worth noting that there are market opportunities for using PTX-100 in drug combinations, something the excellent safety profile (and

[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8235949/
[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5218629/
[8] Source: *Most expensive drugs in the US in 2023* by Fraiser Kansteiner, Zoey Becker, Angus Liu, Eric Sagonowsky and Kevin Dunleavy, Fierce Pharma, 22 May 2023.
[9] J Clin Oncol. 2011 Mar 20; 29(9): 1182–1189. Published online 2011 Jan 18.
[10] https://pubmed.ncbi.nlm.nih.gov/23008944/
[11] In 2022 North America accounted for around 52% of world pharmaceutical sales. Source: EFPIA, *The Pharmaceutical Industry in Figures, Key Data 2023*.

efficacy) would lend itself to, opening up additional clinical and commercial opportunities.

What's next for PTX-100?

PTX-100 is the most advanced asset PTX has. The company is planning a Phase 2 trial and is working with the FDA for it to be an Accelerated Approval Study so that it could be submitted for FDA approval if and when it passed this study without the need for a Phase 3 study. PTX is also expanding the current trial to create a more robust regulatory package.

CellPryme

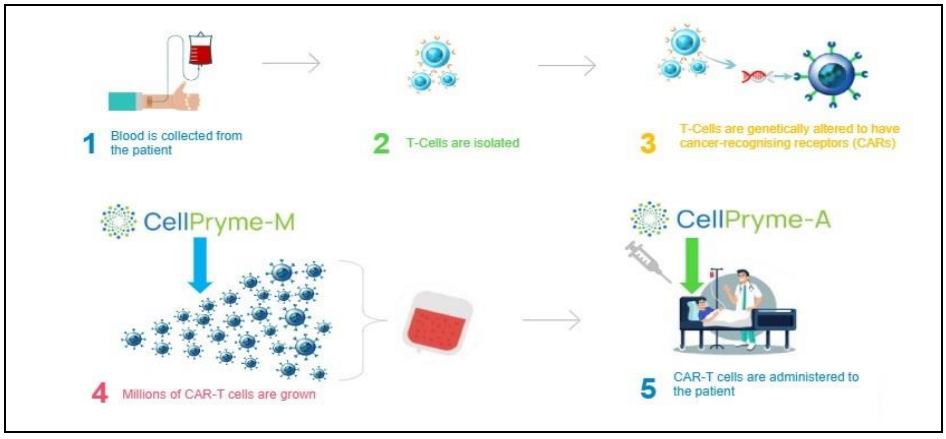
CellPryme is a clinic-ready, high-performance cell therapy enhancement platform that can improve CAR-T efficacy.

CellPryme-M makes for better CAR-T cells while CellPryme-A allows the tumour microenvironment to be overcome.

There are currently two complementary CellPryme applications, CellPryme-M and CellPryme-A, both of which were unveiled in 2022. They can be used both separately or concurrently with both significant power in their own right, and substantial synergies when used together (Figure 3).

To sum these up in a nutshell, CellPryme-M, through the introduction of molecules during a cell manufacturing process, allows better kinds of cells, which improves cellular therapies like CAR-T. CellPryme-A allows the tumour microenvironment to be overcome.

Figure 3: Outline of CellPryme



Source: Company

CellPryme-M

CellPryme-M is a technology that operates during the cell manufacturing process to produce more 'youthful' cells. This technology was developed by PTX in conjunction with the Peter MacCallum Cancer Centre.

CellPryme-M involves introducing molecules during that cell manufacturing process that influences gene expression in immune cells, down-regulating of genes associated with cell metabolism and protein folding and up-regulation of genes associated with interferon and cytokine signalling and genomic stability. The T and NK cells are shifted towards a central memory phenotype.

The result is cells that are less prone to exhaustion, enabling longer duration of cancer killing activity, and are capable of improved tumour trafficking and penetrance compared to the current generation of CAR-T cells. The platform requires minimal intervention into existing and emerging manufacturing processes. Specifically, they have:

- 50% more central memory T-cells, a highly clinically relevant sub-type
- Double proportion of CD4+ helper T-cells, for synergy with effector T-cells
- Significantly more chemokine receptors, important for tumour trafficking and tumour penetrance and especially important in solid tumours, and
- Greater genomic stability and DNA repair for enhanced self-renewal.

Importantly, the superior cell phenotype of CellPryme-M cells does not come at the expense of effectiveness, with T-cells retaining their potency with no increased safety risks due to higher cytokine release. Pre-clinical data has been promising and has been replicated in three separate experiments. In a mouse model of highly aggressive breast cancer that was largely resistant to conventional CAR-T, CellPryme-M CAR-T cells nearly doubled tumour control compared to conventional CAR-T and significant improved survival. Recently, PTX showed that CellPryme-M could improve the *in vivo* function of CAR-T cells expanded in IL2/7, and these outcomes were superior to those achieved by CAR-T cells expanded in IL7/15, which is the current industry standard for promoting enrichment of central memory T cells[12].

PTX plans to partner and license it to other companies with CAR-T or other cell therapy programs to enhance the performance of these therapies, particularly those that are struggling with tumour penetrance with their CAR-T cells. Any cell therapy that could benefit from additional productivity in manufacturing or increased potency and durability in-vivo would be good candidates.

CellPryme-A

CellPryme-A is an intravenous drug administered alongside cellular immunotherapy (either before or alongside it), to address the hostile tumour microenvironment that cellular immunotherapies face. PTX unveiled CellPryme-A three months after CellPryme-M, at the CAR-TCR Summit in Boston.

In vivo, CellPryme-A conquers suppressive regulatory T-cells (Tregs) surrounding solid tumours that counteract the effectiveness of CAR-T and other cancer therapies by infiltrating into the tumour. Tregs are some of the most immunosuppressive immune cells in the body, prohibiting efficient tumour killing through the release of immunosuppressive cytokines and alterations in metabolic demand.

CellPryme-A:

- Significantly decreases suppressive regulatory T-cells;
- increases expansion of CAR-T cells 9-fold *in vivo*; and
- increases tumour penetration of CAR-T cells four-fold.

Just as is the case with CellPryme-M, it is both an opportunity to enhance its own therapies as well as a potential business opportunity through collaboration with external parties.

[12] Cytokines Interleukin-2IL-2, IL-7 and IL-15 have been found to stimulate the growth of T cells, however, the optimised combination of these three cytokines for T cell proliferation is still being worked out by researchers.

What's the market opportunity for CellPryme?

There are numerous cell therapy products that can benefit from CellPryme. Consider that there are currently more than 3,600 CAR-T programs (not to mention other cell therapies like NK) currently in development. This represents the total potential addressable market for CellPryme. CellPryme-M could be sold as a high-performance reagent to cell manufacturers.

For CellPryme-A, there are almost 1,000 CAR-T clinical trials, not to mention those therapies already approved. CellPryme-A could command significantly higher price as a therapy to be administered to patients alongside cell therapies.

What's next for CellPryme?

CellPryme is now ready for the clinic, with GMP material already available. Prescient is preparing requisite regulatory documentation to move its first products into clinical development. We also look to see commercial partnerships on CellPryme-M, while for CellPryme-A we look for collaboration partners.

OmniCAR and the CAR-T Revolution

Why adoptive cell therapy and CAR-T represent a significant step forward in cancer treatment

There is a need for new treatments for cancer that further improve survival and reduce the cancer burden while inducing lower systemic toxicity.

While surgery, chemotherapy and radiotherapy have undeniably had some success in reducing cancer-related mortality, they can cause severe side effects, caused by collateral damaging of healthy tissues, and do not always work. As a result, biotech companies around the world have sought for new treatments that further improve survival and reduce the cancer burden while inducing lower systemic toxicity.

Immunotherapy in general is an approach that uses antibodies, cytokines, and immune cells to modulate the host immune response to cancer. Adoptive Cell Transfer (ACT) is a type of immunotherapy approach that had gained traction in recent years. It is based on the infusion of lymphocytes, usually autologous T-cells, to fight disease in patients. By selecting or modifying the lymphocytes specificity towards a target antigen, they are expanded and injected back into the patient, where they exert their cytotoxic activity and help to mount a sustained immune response against it.

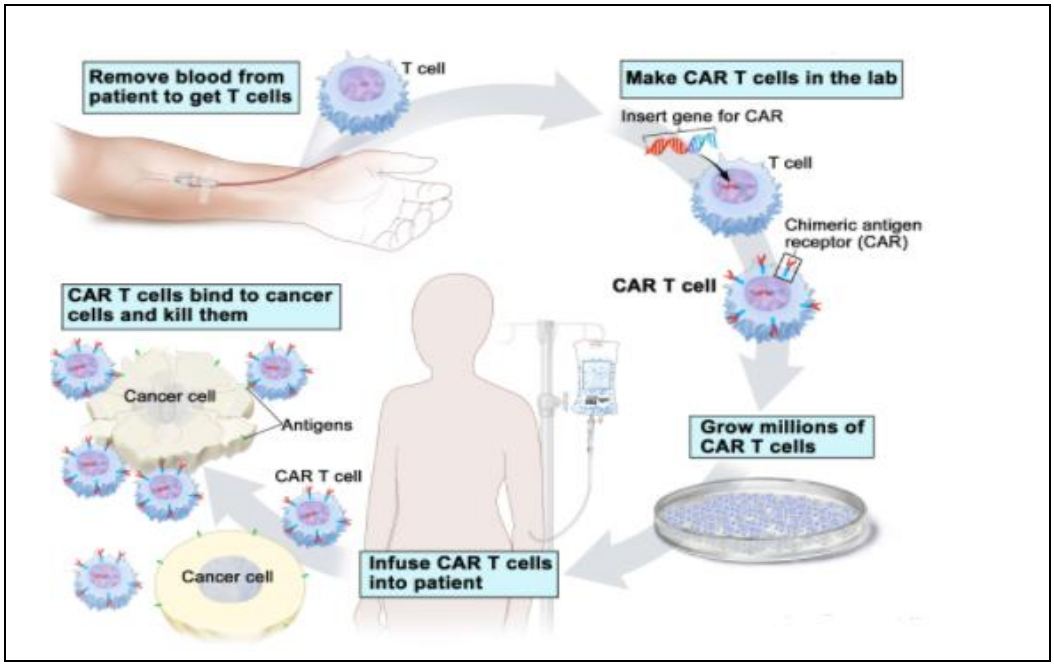
CAR-T cell therapy is unique in using the body's own T-cells.

One type of ACT is Chimeric Antigen Receptor (CAR) T-cell therapy[13]. CAR-T is unique in using the body's own T-cells, which are isolated from the patient's peripheral blood, endowed with enhanced specificity and killing efficacy towards the patient's cancer cells, and then reinjected into the host, where they aid in tumour clearance (Figure 4). This occurs through the genetic modification of the T-cells, so they express the CAR (a receptor engineered to recognise a given antigen of the patient's cancer cells) and activate the CAR T-cells expansion and cytotoxic potential upon recognition[14].

Clinical data over the last decade shows that this technique providing extended periods of disease remission, making it a very promising cancer treatment. Indeed, three of the six treatments on the market today (Kymriah, Tecartus and Abecma) have shown remission rates of over 80%[15].

[13] See *CAR-T Cells: Engineering Patients' Immune Cells to Treat Their Cancers*, National Cancer Institute, 30 July 2019.
[14] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10094630/
[15] Ibid.

Figure 4: CAR-T cell therapy mechanism



Source: National Cancer Institute

How CAR-T therapy works

The CAR involved in CAR-T cell treatment is composed differently depending on the target and CAR-T cell generation. The key steps involved in this therapy (Figure 2) are as follows:

1. **Collection of T-cells from the patient**. T-cells are obtained through a technique that involves drawing blood from the body and separating one or more blood components, such as plasma, platelets, or white blood cells. Thereafter, the remaining blood is returned to the patient's body.
2. **Reengineering T-cells in the laboratory**. T-cells are then genetically engineered in a laboratory by introducing DNA that will help in the production of CARs on the cell surface. These reengineered cells are now known as CAR-T cells. This stage of the process (and the next one) can take up to a fortnight altogether.
3. **Multiplication of reengineered CAR-T cells**. The reengineered CAR-T cells are multiplied in the laboratory and the frozen cells are then transferred to the hospital or trial site where the patient is being treated.
4. **Infusion of CAR-T cells into the patient's body**. In the hospital, the patient is given a brief course of chemotherapy before the infusion of CAR-T cells into the body. This chemotherapy is a specific type of chemotherapy that targets these immune cells and allows for greater CAR-T cell expansion, persistence post-infusion and greater antitumoral efficacy. Then the CAR-T cells are infused intravenously. Although no biotech company has confirmed this, academic research has estimated that around 100 million variable CAR-T cells are infused. Thereafter, the CAR-T cells are expected to recognise and attack cells that have the targeted antigen on their surface.

The key merits of this therapy are as follows:

- **High efficacy**: CAR-T cell therapies have higher reactivity with cancer than existing treatments.
- **High specificity**: CAR-T cell therapies are specifically engineered to identify and kill tumour cells.
- **Long-term benefits**: CAR-T cell therapies have the potential to enhance immune memory against cancer cells[16].

CAR-T cell therapy market to expand significantly

The global CAR-T treatment market is valued at US$33.1bn.

PTX is seeking to conquer a substantial market opportunity. The global CAR-T treatment market is valued at US$33.1bn, according to TechSci Research. This is expected to grow as types of cancers are targeted that have been less prominent, but that CAR-T can help with, such as T-Cell Lymphoma.

While the currently approved CAR-T therapies have helped revolutionise cancer treatment, they remain inaccessible to many due to high costs and have some shortcomings which we will address on the next page. The six CAR-T therapies currently approved by the FDA are as follows:

- **Kymriah**: Novartis' Kymriah was the first CAR-T therapy product approved by the FDA in August 2017 for refractory or relapsed diffuse large B-cell lymphoma in adults (DLBCL) over 25 and for relapsed or refractory acute lymphoblastic leukemia in young adult patients up to 25. The study that led to the approval of Kymriah demonstrated an overall remission rate of 81%17 within three months. Kymriah registered sales of US$264m in the first half of 2023.
- **Yescarta:** Yescarta, developed by Kite Pharma (now a subsidiary of Gilead), gained FDA approval in October 2017. Fast forward to 2022 and it had reached sales of more than US$1bn. It is for patients with 5 specific types of lymphoma (one of which is DLBCL) that have either not responded to or have relapsed following two or more lines of systemic therapy.
- **Tecartus:** Kite Pharma has another CAR-T therapy product, Tecartus18, which received FDA approval for relapsed or refractory mantle cell lymphoma in July 2020. It is also approved for adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).
- **Breyanzi:** Bristol-Myers Squibb received FDA approval for its CAR-T product, Breyanzi, in February 2021 for the treatment of DLBCL. It is worthwhile to mention that when Celgene acquired Juno Therapeutics for US$9bn in January 2018, it predicted peak sales of US$3bn 19 for Breyanzi. Thereafter, in late 2019, Celgene was acquired by Bristol-Myers Squibb.
- **Abecma:** Developed by Bristol-Myers Squibb and approved by the FDA in March 2021. It is for adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. It has guided to $470-570m sales in 2023.

[16] See *CAR-T Cell Therapies Market (3rd Edition),* Root Analysis Business Research & Consulting, March 2021.
[17] N Engl J Med. 2018 Feb 1;378(5):439-448.
[18] Generic name brexucabtagene autoleucel, see tecartus.com.
[19] See the Celgene press release dated 22 January 2018 and headlined '*Celgene Corporation to acquire Juno Therapeutics*'.

- **Carvytki**: Developed by Janssen Biotech. It is for patients with relapsed or refractory multiple myeloma after four prior lines of therapy and was FDA approved in February 2022.

Challenges with CAR-T

Despite the benefits of CAR-T, there are challenges that have inhibited the commercial rollout of these therapies.

Despite the benefits of CAR-T, there are challenges that have inhibited the commercial rollout and broader adoption of all these therapies. Granted, they have not stopped their approval, but they will (at least for some time) hold therapies back from reaching their full commercial potential (Figure 5).

Figure 5: CAR-T challenges

	Challenge
Safety / Control	No control post infusion
Targeting	Difficulties with targeting, antigen heterogeneity
Escape	Difficulties with mutating antigens
Production efficiency	Cost prohibitive & slow
Exhaustion	Cells run out of steam
Trafficking	Cells cannot find their way
Tumor penetrance	Protective layer around tumor
Tumor microenvironment	Suppresses immune cells

Source: Company

There are two that we would like to highlight. The first of these is cost - industry experts estimate that CAR-T therapy costs up to ~US$1-1.5m in the US, including administration and hospitalisation costs[20]. A single treatment of Yescarta comes with a price tag of US$475,000 per patient[21] – exclusive of the costs we noted beforehand. With this price tag, insurance approval for CAR-T will continue to be a long-drawn process, particularly in the US. The high expense associated with the therapy may make it impractical for large-scale adoption in the future, if other existing treatments offer better value as first-line options in cancer treatment. Further CAR-T cell therapies coming onto market could help resolve the issue of healthcare reimbursements associated with CAR-T cell therapies.

The second is that normally with CAR-T, a single cell targets a single antigen, and the T-cell activity, is not controllable once it is 'unleashed'. As we will outline in this report, OmniCAR allows solutions to both these problems to be created.

[20] It is unknown where this original estimate came from, but in the cancer oncology space it is considered common knowledge.
[21] Source: drugs.com.

OmniCAR: PTX's unique approach to CAR-T

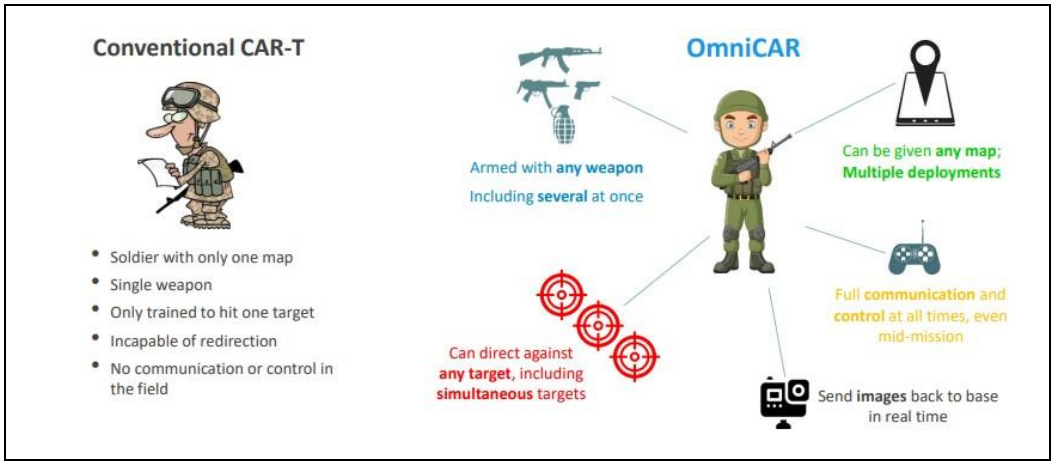
OmniCAR is basically two technologies combined into the same platform: A universal immune receptor platform developed at the University of Pennsylvania in the laboratories of Dr Daniel Powell and Dr Andrew Tsourkas; and a molecular binding system developed at Oxford University called 'SpyTag/SpyCatcher'.

PTX picked up this platform in May 2020 and has been working on it ever since.

Why OmniCAR is potentially more powerful that current CAR-T

As complicated as cancer technology is, we think the below cartoon (Figure 6) composed by the company in May 2020 when it unveiled the purchase is the perfect illustration of how OmniCAR is superior and more powerful.

Figure 6: How OmniCAR is more powerful



Source: Company

OmniCAR separates the two domains but then connects them up through two molecules that can covalently bond.

We think the two benefits which are most important are:

1. That while conventional CAR-T can only start an anti-cancer immune response, OmniCAR can stop it if necessary, then restart it if desired.
2. The ability to target multiple antigens.

Both factors come down to how the 'signalling domain' and the 'targeting domain' of the antigen receptor are treated.

Addressing the second of these first - with 'conventional' CAR-T cells, these are combined in a single construct that is then spliced into the patient's T-cells. The targeting domain zeroes in on the cancer cell while the signalling domain tells the T-cell to initiate an immune response against the cancer cells.

OmniCAR simply separates the two domains but then connects them up through two molecules – SpyTag on the targeting ligand and SpyCatcher on the signalling domain fused to the T-cell – that can covalently bond. That means that more than one targeting domains can be used, allowing the targeting of multiple antigens.

Turning our attention back to the first benefit: the beauty of separating the 'signalling domain' and the 'targeting domain' and then connecting them up with SpyTag/ SpyCatcher is that if the therapy starts a 'cytokine storm' that is

potentially life-threatening to the patient, the doctors can simply cease administration of the targeting ligand, thereby switching off the therapy.

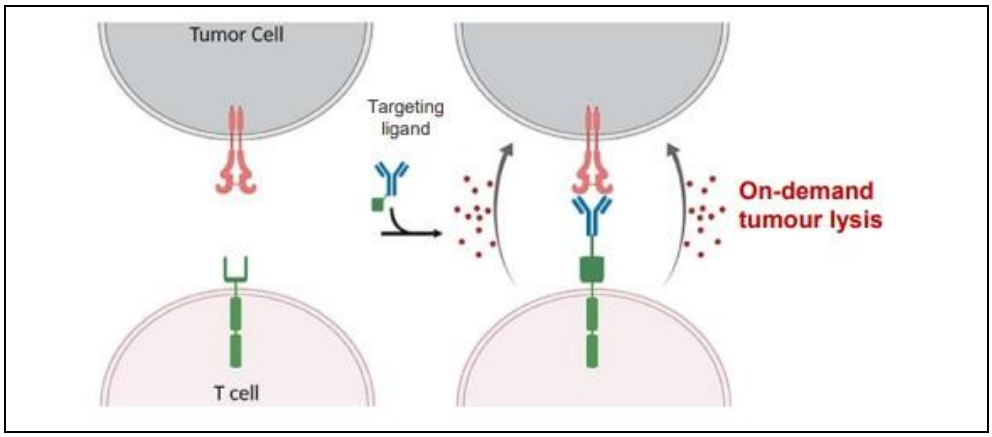
How does it work?

It is a three-step process:

1. Unarmed (and inactive) CAR-T cells are administered to the patient.
2. Separate administration of targeted ligand results in a complete, armed CAR-T cell
3. Armed CAR-T cells are activated, resulted in on-demand tumour killing.

From here, CAR-T cell activity is now controllable. Target specificity CAR-T cell can be switched at will for whatever reason (including if it needs to be adjusted for safety and efficacy reasons), by administering a different targeting ligand (Figure 7).

Figure 7: How OmniCAR is more powerful



Source: Company

What is next?

Prescient is progressing pre-clinical development of the OmniCAR platform, seeking to optimise various features.

Valuing PTX

We value PTX at 11.6c per share in our base case and 16.3c per share in our bull case.

Using a Sum of the Parts rationale (with 2 risk-adjusted DCFs for PTX-100 and CellPryme), we value PTX at 11.6c per share in our base case and 16.3c per share in our bull case (Figures 8 & 9). Our total valuation of PTX is the sum of the NPV of PTX-100 and CellPryme as well as the company's net cash position (worth 0.7c per share).

Our valuation attributes 65% of the company's value to PTX-100 and 30% to CellPrume – the gap primarily due to the more advanced stage PTX-100 – with the balance being the company's cash position. Our assumptions are outlined below and summarised succinctly in Figure 9.

PTX-100

We assume that this asset is commercialised in CY28 and model 10 years thereafter (with no terminal growth thereafter assumed). This assumes that PTX navigates all necessary clinical stages for approval and is successful in getting FDA approval. We assume it strikes a deal with a commercial partner before the end of the current clinical trial with upfront fees of up to $36m (derisked) and the right to keep all revenues bar a royalty to PTX (which we assume is 20% of sales in our base case). Our base case assumes a market of 5,500 patients per annum (the midway point of the market now as outlined in the previous section) while our bull case assumes 6,500. Our price is US$450,000 per patient using Acrotech Biopharma's Folotyn as a guide. We assume that by the end of the life of our model, it can reach 50% of these patients. Sales peak at $2.5bn in our base case and $3.5bn in our bull case.

Our NPV is US$38.4m in our base case, equating to A$60.9m using a 63c AUD/USD exchange rate which equates to 7.6c per share. Our bull case derives an NPV of US$54.4m, equating to A$86.3m or 10.7c per share. Our 16.2% discount rate is derived from a 4% risk free rate of return, an 8% equity premium and a 1.5x beta. We have used a further weighted probability of 30%.

CellPryme

We anticipate a near-term revenue opportunity for CellPryme-M in selling to potential manufacturers. However, for conservatism's sake, we value CellPryme as a key part of an approved breast cancer treatment, since this the most advanced pre-clinical indication at present. We modelled the breast cancer market as being 242,100 patients (as per CDC data). We again assume US$450,000 per treatment and assume commercialisation in CY31 and model 7 years of royalty revenues thereafter. Note that this model for CellPryme is illustrative, and we expect will evolve over time.

Given the size of the market, we only assume a 2.5% peak market share in our base case and 3% in our bull case but use the same royalty assumptions (20%) and cost assumptions (50% of royalty sales in our base case and 45% in our bull case) as we did with PTX-100. Our final revenues are weighted with a 15% probability factor and then modelled post a 21% corporate tax rate (as per the rate in the USA) and a 16.2% discount rate.

Our NPV is US$17.0m in our base case, equating to A$27.1m using a 63c AUD/USD exchange rate which equates to 3.4c per share. Our bull case derives an NPV of US$25.1m, equating to A$39.9m or 5.0c per share.

Figure 8: Our valuation of PTX

Sum of the Parts Valuation	Base Case		Bull case	
Drugs	**A$m**	**A$ps**	**A$m**	**A$ps**
PTX-100	60.52	0.075	85.78	0.107
CellPryme	27.06	0.034	39.91	0.050
rNPV	**87.57**	**0.109**	**125.69**	**0.156**
Cash (close of FY23)	5.89543	0.007	5.89543	0.007
Debt (close of FY23)	-	-	-	-
Equity Value	**93.47**	**0.116**	**131.58**	**0.163**
Current Price		0.056		0.056
Upside		107%		192%

Estimates: Pitt Street Research

Figure 9: Our key DCF assumptions

DCF Assumptions (Base case)	PTX-100	CellPryme
Launch	CY28	CY31
Estimate market size (patient numbers)	5,500	242,100
Growth	2%	1%
Potential market penetration	50%	1%
Realised price (US$)	450,000	450,000
Peak sales (US$m)	2,595	3,528
Peak royalty revenue (US$m)	519	706
Gross milestone revenue (US$m)	75	40
Commercial exclusivity period (years)	10	7
Drug development cost (US$m)	40	58
Partner's share of costs	50.0%	50.0%
Discount rate	16.2%	16.2%
Royalty rate	20.0%	20.0%
Tax rate	21.0%	21.0%
Probability of success	30.00%	15.00%
Risk-adjusted NPV (A$m) - base case	60.52	27.06
rNPV per share (A$) - base case	0.075	0.034

Estimates: Pitt Street Research

Key risks facing PTX

Risks specific to PTX. We see the following major risks for PTX 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.
- **Technical risk.** Some of the technologies that PTX is working with are relatively new and therefore may not therefore be 'bug-free'.
- **Regulatory risk**. There is the risk that regulators may decline to approve PTX products, even if PTX considers the data submitted to be adequate.
- **Commercial risk**. There is the risk that PTX may fail to find commercial partners for its products.
- **Uptake risk**. There is the risk that PTX 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 PTX.

Companies in cellular therapies

2seventy bio (NDQ:TSVT) – 2seventybio is a Massachusetts-based company responsible for the Abecma cancer cell therapy. Abecma is a CAR T-cell therapy for multiple myeloma. In August 2022, the company (in conjunction with Birstol Myers Squibb) announced positive results from a Phase 3 trial using Abecma. The study, the first of its kind to evaluate a CAR T-cell therapy for multiple myeloma, met its primary endpoint of demonstrating a statistically significant improvement in progression-free survival.

Adicet Bio (NDQ:ACET) **–** Adicet has a pipeline of products in clinical and pre-clinical studies. Its two lead products are ADI-001, a therapy targeting Non-Hodgkin's Lymphoma that is in late Phase 1, and ADI-002 which is also in Phase 1 and has been licensed to Regeneron Pharmaceuticals. Adicet's portfolios employ gamma-delta T-cells rather than alpha-beta T-cell receptors.

Allogene Therapeutics (NDQ:ALLO) – Allogenic's CAR-T niche is using T-cells from healthy donors, in other words allogeneic cell therapy rather than autologous cell therapy. It manufactures cells enmasse, engineers them to express CARs to recognise and destroy cancer cells and modified via gene editing to limit an adverse autoimmune response when given to a patient. It is currently operating several clinical programs, 2 of which are in Phase 2.

Anixa Biosciences (NDQ:ANIX) – Anixa's CAR-T approach is known as chimeric endocrine receptor T-cell (CER-T) since the target of the engineered T-cells is an endocrine receptor. It cleared IND application in 2021 and is currently undertaking a clinical trial at Moffitt Cancer Center targeting ovarian cancer.

Arcellx (NDQ:ACLX) – Arcellx's lead product candidate is CART-ddBCMA which is being developed for the treatment of relapsed or refractory multiple myeloma (rrMM). It is currently in a Phase 2 clinical trial in conjunction with Kite Pharmaceuticals, owned by Gilead and it is expected that Kite will commercialise the product outside the US with a Joint venture between the companies to oversee commercialisation in the US. The trial was temporarily paused earlier this year after the death of a patient was investigated. A commercial launch is estimated for 2024 with preliminary data expected at the end of 2024.

Autolus Therapeutics (NDQ:AUTL) – Autolus has a range of T-cell therapies in the pipeline for the treatment of hematological malignancies and solid tumours. Its lead asset is AUTO4, a candidate for T-Cell Lymphoma. AU4 is currently in a Phase 1/2 study that reported positive interim data in June.

Gracell Biotechnologies (NDQ:GRCL) – This Chinese headquartered company has both autologous and allogenic products in the clinical pipeline with its FasTCAR and TruUCAR technology platforms. It is hoping to increase the speed of production and reduce costs of CAR T therapies through its therapies through FasTCAR, which automates the manufacturing process in a closed-loop clean suite facility to manufacture several patient samples simultaneously. In 2023, it obtained an IND application in the US and commenced a clinical trial evaluating its GC012F for the treatment of multiple myeloma.

Intellia Therapeutics (NDQ:NTLA) – Intellia is a gene editing firm. Its gene therapy NTLA-2002 commenced a mid-stage trial in March 2023 targeting hereditary angioedema (HAE). It uses the gene-editing tool CRISPR to reduce the level and activity of the inflammation-causing gene, kallikrein B1 (KLKB1).

Nkarta (NDQ:NKTX) – Nkarta's technology utilises natural killer (NK) cells to treat cancer. It is in an early-stage study against acute myeloid leukemia and

shareholders have been anxious about results released in June because the remission rate was lower than the year before.

Poseida Therapeutics (NDQ:PSTX) – Posedia is a San-Diego based company with P-MUC1C-ALLO1, an allogeneic CAR-T cell therapy being developed for solid tumours derived from epithelial cells as well as any other cancers expressing a cancer-specific form of the Mucin 1 protein. Earlier in 2023, it sold an 8.8% stake to the major Japanese pharma company Astellas in a deal that may see the pair partner for the current flagship therapy and others down the track.

Precigen (NDQ:PGEN) – Precigen is based in Germantown, Maryland and after bein formed in 1998 as Intrexon, rebranded itself in 2020 after its gene therapy subsidiary. It has the UltraCAR-T platform and a therapy known as PRGN-3006 that it hopes to treat acute myeloid leukemia with. It signed an exclusive license agreement with Alaunos Therapeutics back in April 2023.

Companies in rare disease therapeutics and precision medicine

Affimed (NDQ:AFMD). This company develops bispecific antibodies that can bind tumour cells to either T cells or NK cell. The company's lead candidate is AFM13, which binds the cancer antigen CD30 and the CD16A antigen on NK cells. This product has completed Phase 2 in Peripheral T cell lymphoma and is in Phase 1/2a in CD30-positive lymphoma.

Annexon Biosciences (NDQ:ANNX). This company designs drugs that inhibit C1q, the initiating molecule of the complement cascade, useful in CNS diseases as well as inflammatory disorders. The company's ANX005 drug is in Phase 3 in Guillain-Barré Syndrome and Phase 2 in Huntington's Disease while ANX007 is in Phase 2 in Geographic Atrophy, a form of macular degeneration.

Arcturus Therapeutics (NDQ:ARCT). This company has been built on technology for lipid-mediated drug delivery, allowing better deliver of mRNA therapeutics. Arcturus' pipeline includes an RNA therapeutic for ornithine transcarbamylase deficiency and cystic fibrosis, along with its partnered mRNA vaccine programs for Covid-19 and influenza.

Avidity Biosciences (NDQ:RNA). This company's Antibody Oligonucleotide Conjugates (AOCs) combine the specificity of monoclonal antibodies with the precision of oligonucleotide therapies. Having shown it was possibly with AOCS to do targeted delivery of RNA into muscle, the company now has early-stage clinical programmes in myotonic dystrophy type 1 (DM1), Duchenne muscular dystrophy (DMD) and facioscapulohumeral muscular dystrophy (FSHD).

Relay Therapeutics (NDQ:RLAY). This company's Dynamo platform integrates computational and experimental approaches to discover new candidates for targets that have yet to be properly drugged. The company's lead compound is RLY-4008, a small molecule inhibitor of FGFR2, a receptor tyrosine kinase. This drug is currently in Phase 1/2 in advanced solid tumours.

Sangamo Therapeutics (NDQ:SGMO). This company was built on 'zinc finger proteins', naturally occurring molecules that are involved in genomic regulation and from which Sangamo develops genomic medicines. The company's lead programme, now in Phase 3, is Giroctocogene fitelparvovec, a genomic medicine to replace F8, the gene which causes Hemophilia A.

Ultragenyx Pharmaceutical (NDQ:RARE). This company has a pipeline of drugs to treat rare and ultrarare diseases, spanning traditional biologics, small molecules, gene therapies, or nucleic acid therapies. Some of these are marketed products. For example., Ultragenyx gained FDA approval of Dojolvi (UX007/triheptanoin), the first FDA-approved therapy for the treatment of long-chain fatty acid oxidation disorders, in 2020. Others, such as UX143 (setrusumab) for Osteogenesis imperfecta, are in Phase 3.

PTX's leadership team

PTX has the ideal leadership team to advance its clinical programs. The current board members are listed below (Figure 10):

Figure 10: PTX's Board members and senior management

Name and Designation	Profile
Steven Yatomi-Clarke CEO and Managing Director	• Steven has led PTX since 2016 and has overseen its progression ever since. • Mr Yatomi-Clarke manages a team in Australia and the US and has been instrumental in strategy development; licensing; initiating and managing clinical trials; fundraising and business development. • Previously, he had a distinguished career as an investment banker specialising in the life sciences sector, where he was consistently one of the country's most prolific bankers, involved in primary and secondary offerings, corporate advisory and M&A assignments. • Mr Yatomi-Clarke holds a Bachelor of Science with an Honours Degree in Biochemistry and Molecular Biology, and a Bachelor Commerce majoring in Economics, both from the University of Melbourne. He has been a collaborator on various immunotherapy research projects.
Steven Engle Independent Non-Executive Director	• Steve has over two decades of executive leadership experience with US public biotech companies developing breakthrough products in the metabolic, autoimmune, oncologic and infectious disease areas, including XOMA and La Jolla Pharmaceuticals • Mr. Engle holds M.S.E.E. and B.S.E.E. degrees from the University of Texas with a focus in biomedical engineering.

Dr James Campbell Independent Non-Executive Director	• Dr Campbell has a solid track record as a scientist and commercial executive with more than 20 years of international biotechnology research, management and leadership experience. He has been involved in the creation and/or transformation of multiple successful Australian and international biotechnology companies. • He is currently CEO of Patrys Limited, a company developing novel antibody therapeutics for oncology. He was previously the Chief Financial Officer and Chief Operating Officer of Chemgenex, which was acquired by Cephalon for $230 million in 2011. His responsibilities ranged from IP management to licensing and business development and as a member of the executive team, he helped steer and transform the company from a $10 million research-based entity to a company with completed clinical trials and regulatory dossiers submitted to the FDA and EMA before its $230 million sale. • Dr Campbell also has experience advising private biotechnology companies in the US and New Zealand with capital raisings and partnering negotiations.
Dr Ellen Feigal Independent Non-Executive Director	• Dr Feigal joined PTX's board in May 2023. She is an accomplished industry leader with a strong track record in commercialising new cell-based treatments. • Dr Feigal brings a depth of experience in the commercialisation, product development and regulatory strategies of cell therapies, hematology and oncology with her career spanning leadership roles in industry, academia and non-profits. • She is a partner and head of the Biologics practice at global life sciences advisory firm NDA Partners. She is also adjunct faculty at the Sandra Day OÇonnor College of Law at Arizona State University where she teaches FDA drug law and medical research ethics and law.
Dr Allen Ebens Non-Executive Director	• Dr Ebens, Ph.D. brings over twenty-four years of drug development experience in oncology and hematology, beginning in drug discovery at Exelixis before moving to Genentech where over 11 years he worked from concept to clinic across multiple therapeutic platforms including antibodies, small molecule drugs, antibody-drug conjugates, andT-cell recruiting antibodies. • Dr. Ebens was recruited from Genentech to establish oncology discovery research at Juno Therapeutics (a CAR-T pioneer), and served as Senior Director, Immune Oncology at NGM Biopharmaceuticals. Ebens' scientific contributions include numerous peer-reviewed publications of original research, a significant patent portfolio, and the advancement of nine discovery projects from initial concept to clinical development for multiple targets including one marketed therapeutic. He completed his PhD at UCLA and postdoctoral training at UCSF • He is currently Chief Scientific Officer of Vera Therapeutics.

Melanie Leydin CFO and Company Secretary	• Melanie is a highly experienced CFO and Company Secretary with 25 years of experience in the accounting profession and 15 years of experience in company secretarial services

Appendix I – PTX-200

PTX-200 is another intravenous anti-cancer drug that works as a so-called AKT inhibitor that is targeting breast cancer and AML. PTX-200 is an Orphan Drug in AML, having obtained that status in May 2017.

The PI3K/AKT/mTOR pathway is one if the more important cellular signalling pathways in cancer, sitting as it does at the centre of multiple pathways and playing a role in many tumour types. AKT contributes to chemoresistance in many cancers.

PTX-200 works as a so-called AKT inhibitor that is targeting breast cancer and AML.

Pre-clinical work on PTX-200 has shown a high level of specificity for just AKT with no off-target effects. It achieves this by binding to AKT's PH domain and preventing it from localising in the plasma membrane where it can be activated.

In 2023 PTX-200 is non-core for Prescient. While the data for PTX-200 has been is good, the treatment options for patients with Acute Myeloid Leukaemia have improved markedly in the years since this drug came into PTX's portfolio. There are now over 40 drugs that are FDA approved for AML[22] and there have been 11 approved by the FDA since 2017 alone, although only one combination which is ADE[23] and this is only approved for AML in children[24]. Given this change, Prescient now regards its drug as non-core, and the company has materially reduced investment in this program as the Phase 1b trial in AML concludes.

The history of PTX-200

PTX-200 was patented by Professor Said Sebti at Moffitt Cancer Center. He realised in the early 2000s that Triciribine Phosphate Monohydrate, which had first been tried in cancer in the 1970s but had been abandoned due to variable performance, would be effective against tumours that expressed high levels of AKT. Sebti and colleagues hypothesised that just treating those patients with TCN-P would yield good responses.

By the time the drug came into Prescient's pipeline in 2014 two clinical studies had been initiated – a Phase 1b/2 in breast cancer, and a Phase 1b in ovarian cancer – where the aim was to overcome resistance to platinum-based drugs. A third programme was added in late 2016 when a Phase 1b/2 study commenced in Acute Myeloid Leukemia. The three studies were subjected to a clinical hold in May 2017 due to a death in the breast cancer study however, following a review, the holds were lifted after a few months[25].

[22] National Cancer Institute
[23] Cytarabine (Ara-C), Daunorubicin Hydrochloride and Etoposide Phosphate
[24] https://www.sciencedirect.com/science/article/pii/S0145212623006537?via%3Dihub
[25] September 2017 in Acute Myeloid Leukemia, November 2017 in ovarian cancer and December 2017 in breast cancer.

PTX-200 has generated some great numbers

Prior to PTX-200 coming into Prescient's pipeline the Moffitt and MD Anderson Cancer Center had conducted study [26] that recruited multiple leukemia types. This study showed stable disease in 17 out of 32 patients with Acute Myeloid Leukemia, with three patients seeing their bone marrow blasts reducing by 50% and one patient experiencing a return to normal blood count. There is multiple evidence that the AKT pathway is important in AML7.

- A Phase 1b/2 study of PTX-200 in Her2 negative breast cancer8 was initiated prior to the drug going to Prescient. The study, conducted at the Montefiore Medical Center in New York, recruited 28 patients with Stage IIB-IV disease and evaluated PTX-200 in conjunction with paclitaxel, doxorubicin, and cyclophosphamide. Most of these patients were recruited after Prescient took the study over. 16 patients established the 35 mg/m2 dose, and 12 represented the extension cohort at that dose:
- The Phase 1b part of the study commenced in September 2016 and read out favourable data was released in April 2018. In the 10 patients evaluated the overall response rate was 50%. Of the five patients in this group with locally advanced disease the overall response rate was 100% and the Complete Response rate was 40%.
- An interim durability analysis reported in December 2018 showed that the Phase 1b responses were long-lasting. Of the five patients with locally advanced disease, the Progression-Free Survival number was 27 months.

The trial moved into Phase 2 in April 2017 with the completion of Phase 1b. The first Phase 2a data became available in December 2019 and showed a 91% Overall Response Rate in the first 11 patients, with 2 Complete Responses and 8 Partial Responses.

PTX-200 has registered multiple Complete Responses in Acute Myeloid Leukemia. Prescient initiated a Phase 1b/2 study of PTX-200 in 24 refractory or relapsed Acute Myeloid Leukemia in December 2016. This study, also conducted at the Moffitt9, evaluated PTX-200 with cytarabine, a drug that the pre-clinical work had shown was synergistic with PTX-200.

- In August 2016 the Phase 1b results from 13 patients showed two Complete Responses, which was highly encouraging.
- The Phase 1b study was expanded in August 2018 to explore a combination with low dose cytarabine.
- A third complete response was noted from the Phase 1b study in November 2019. In August 2020 the study went to the next dose of 35 mg/m^2 while 45 mg/m^2 was reached in April 2021. At this dose a fourth complete remission was noted in May 2022.

Prescient has also conducted an ovarian cancer study. This study, at the Moffitt Cancer Center, recruited 15 patients10 and studied PTX-200 in combination with carboplatin. It reported great interim data in December 2019, with 80% of patients (12 out of 15 women) showing a partial response or stable disease. Prescient chose not to pursue this indication into Phase 2 in the US and has yet to move this indication forward.

[26] See Sampath et. al., Leuk Res. 2013 Nov; 37(11): 1461–1467.

Appendix II – Glossary

Acute Myeloid Leukemia (AML) – A blood cancer characterised by proliferation and accumulation of myeloid blasts in the bone marrow that are blocked at various stages of differentiation. The disease is called acute because patients develop abnormal numbers of these cells very quickly.

Adoptive T-cell therapy – Cancer treatment in which a patient's ownT-cells are engineered to increase their cancer-fighting properties, and then returned to the patient.

Allogenic – In the context of stem cell transplants, allogenic transplants use stem cells from donor whose human leukocyte antigens are acceptable matches to the patient's.

Antigen – The 'bad guy' substance that stimulates the immune system to respond to the perceived threat. It is the protein to which antibodies bind.

Autologous – The opposite of allogenic where a person's own stem cells are utilised. A patient's stem cells are collected from the patient, undergo transplant conditioning (being frozen in liquid nitrogen until this can occur) and are then returned to the patient's own body.

Blockbuster – A pharmaceutical drug with more than US$1bn in annual sales.

CellPryme – Prescient's platform technology for creating better quality cellular medicines.

Chimeric antigen receptor T-cells (CAR-T cells) – Chimeric antigen receptor T-cells (also known as CAR-T cells) are T-cells that have been genetically engineered to produce an artificial T-cell receptor for use in immunotherapy.

Complete Response – Elimination of a tumour brought about by a cancer drug.

EGFRvIII – A tumour antigen notable in glioblastoma multiforme.

Glioblastoma – A rare brain cancer that begins in the glial cells that surround and support neurons.

Her2 – The protein targeted by the cancer antibody drug Herceptin which is overexpressed on breast cancer cells.

Lymphoma – A cancer of the lymphocytes which the immune system needs to create T and B cells as well as Natural Killer cells. There are two main types of lymphoma, Hodgkin, and Non-Hodgkin, with Hodgkin Lymphoma being characterised by a particular cell type.

OmniCAR – Prescient's platform technology for creating modular cell therapies.

Orphan Drug – A drug that targets a disease affecting less than 200,000 potential patients in the US. Orphan drug designation provides tax benefits as well as market exclusivity in both Europe and the US.

Partial Response – A partial reduction in tumour size brought about by a cancer drug.

Pathway – A succession of signals between molecules within a cell to carry out the growth and functions of the cell. Well-known pathways include, but are not limited to MYC, PI3K/AKT, WNT and NOTCH.

Progression-Free Survival (PFS) – The length of time a cancer patient undergoing treatment can see no worsening of his or her cancer.

T Cells – White blood cells that are responsible for killing cells infected by viruses (in the case of 'Cytotoxic T-cells') and inducing B lymphocytes to produce antibodies (in the case of 'Helper T-cells').

T-Cell Lymphoma – A form of Non-Hodgkin Lymphoma impacting only T-cells.

Appendix III – Capital Structure

Class	In millions	% of fully diluted
Ordinary fully paid shares	805.3	96%
Options	31.83	4%
Fully diluted shares	**837.13**	

Source: Company

Appendix IV – Analyst Qualifications

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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