NDF RESEARCH

Providing independent research coverage of ASX-listed Life Science companies

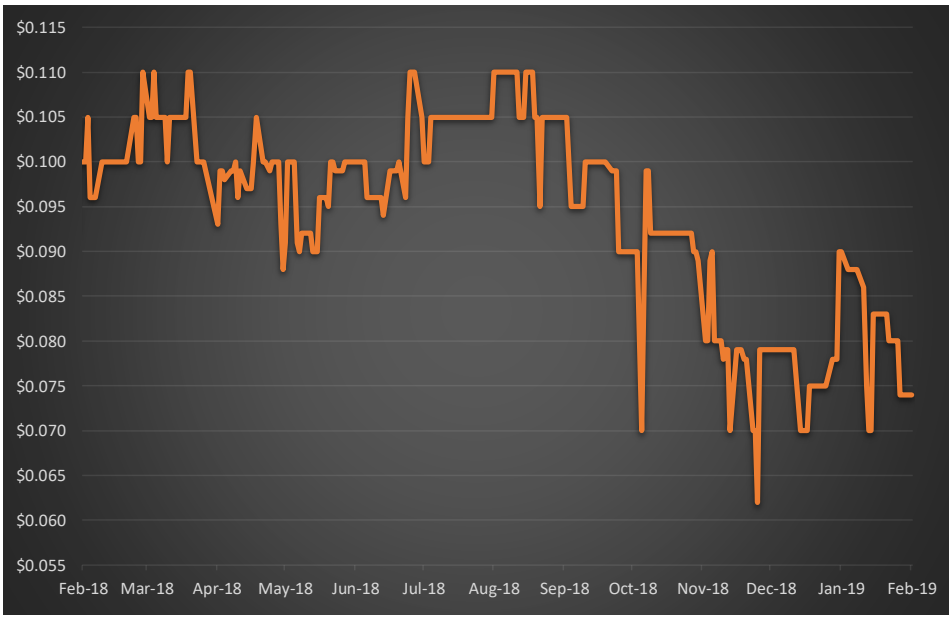
Invitrocue (ASX: IVQ)

Update note – Thursday 7 February 2019

2019: Another year of progress expected for Onco-PDO

This note updates our 20 April 2018 note headlined '*The next step in predicting cancer treatment outcomes*'. Since our initiation report on Invitrocue nine months ago, the company has made progress towards its goal of becoming a leading global provider of cancer treatment prediction services. The flagship Onco-PDO product is now available in Singapore, Hong Kong, Australia and Germany with other markets to follow. Onco-PDO is an affordable but accurate and fast tool for selecting the right drugs from an *in vitro* model of a patient's tumour. With Onco-PDO, the way is open for cost-effective personalised cancer medicine, where the market opportunity lies in the billions. For an idea of the potential upside, consider Roche's June 2018 acquisition of the minority shareholders of the American cancer diagnostics company Foundation Medicine. That transaction valued Foundation, a pioneer of cancer genomic analysis, at US$ 5.3bn. With this note we are maintaining our DCF-based valuation of 7.3 cents base case and 24.4 cents per share optimistic case. Our target price of 16 cents per share sits at the midpoint of our valuation range.

Rating	Risk	Current price	Target price
Buy	Speculative	$0.074	$0.16



Stock details

Daily Turnover: ~A$6,000
Market Cap: A$38.0m
Shares Issued: 513.8m
52-Week High: $0.11
52-Week Low: $0.062

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Please note: This report has been commissioned by Invitrocue and NDF Research will receive payment for its preparation. Please refer below for risks related to Invitrocue as well our General Advice Warning, disclaimer and full disclosures. Also, please be aware that the investment opinion in this report is current as at the date of publication but that the circumstances of the company may change over time, which may in turn affect our investment opinion.

About NDF Research

NDF is an independent equity research firm based in Sydney, Australia. It focuses on Life Science companies that are publicly traded on the Australian Securities Exchange (ASX), most of which are headquartered in Australia and New Zealand. ASX hosts one of the world's premier equity markets for biotech and medical device companies and is home to world-beating companies such as CSL and ResMed and emerging pioneers such as Mesoblast and Impedimed.

NDF's Founder and Senior Analyst, Stuart Roberts, has been involved in Life Sciences since 2002 as a sell-side analyst as well as an executive of two ASX-listed immuno-oncology drug developers.

NDF believes that ASX-listed companies have been largely overlooked in the global Life Sciences boom that began in late 2008, partly because of insufficient quality research. NDF's goal is to provide such research and introduce investors around the world to potential future billion-dollar companies from 'Down Under'.

To learn more about the Life Sciences sector on the ASX and our firm, please visit ndfresearch.com.

Ferry at the end of a rainbow on Sydney Harbour, August 2014

In this report

2019: Another year of progress expected for Onco-PDO

Invitrocue is taking Onco-PDO into new markets. At the time of our April 2018 initiation report on Invitrocue, the company had just screened its first commercial customer for Onco-PDO in Singapore, having spent the previous two years testing the product clinically and developing the relevant lab infrastructure. Since April 2018 the company has worked primarily on setting up new labs that can handle Onco-PDO. Invitrocue has only earned modest amounts of revenue from the product to date, but we expect that it can reach 'take-off' over the next couple of years as the early patients help generate further data on the clinical effectiveness of the product.

Singapore provides a good testbed for Onco-PDO. Invitrocue only started marketing Onco-PDO to the oncology community in Singapore a little less than a year ago, following on from its early treatment successes as published in *Nature Communications* in September 2017[1]. Through 2018 the company consistently enjoyed revenue of A$140,000 per quarter, primarily from Singapore from a continuous increase in Onco-PDO tests. We believe these early patients will allow Invitrocue to further refine the Onco-PDO service offering, as well as generate further published data on the effectiveness of Onco-PDO as a cancer treatment prediction engine.

INVITROCUE HAS ENJOYED STEADY PATIENT FLOW FOR ONCO-PDO

Onco-PDO is now available for patients in Singapore, Hong Kong, Australia and Germany, with other European and Asian markets to follow. During 2018 Invitrocue's senior management was largely focused on setting up labs in other regions. This effort has yielded fruit over the last several months:

- The Singapore lab started accepting patients from Hong Kong shortly after the first local commercial patient was screened.
- The company announced in January 2019 that Systasy Bioscience in Munich[2] would become the first Onco-PDO lab in Germany. That lab is now up and running.
- There are plans to have more labs in the future in key strategic markets in Europe and Asia.

We expect a new kit-based form of the product this year. We expect that towards the end of 2019 Invitrocue will have completed work on the kit-based form of Onco-PO and then then seek 510(k) approval in the US market followed by CE Mark in Europe.

Invitrocue continues to build its team. As Invitrocue has matured as a company, it has continually added to its talent base.

- Professors Jesus Garcia-Foncillas and Masakazu Toi have joined as Clinical Advisors, allowing key opinion leaders in Spain and Japan respectively to be reached with the Onco-PO story.
- Dr Christian Peschel, an authority on tumour biology at the Klinikums rechts der Isar (a hospital affiliated with Technical University of Munich), joined Invitrocue's Scientific Advisory Board
- The medical device veteran Gary Pace, who was an early director of Resmed, was named an Invitrocue director in October 2018.

[1] Nat Commun. 2017 Sep 5;8(1):435.
[2] See www.extassay.com.

We think this activity shows that Invitrocue is gaining ground in terms of support for the Onco-PDO concept, which can gradually allow a step-up in users once the new laboratories are in place.

The Foundation transaction points to the upside for Invitrocue. In our April 2018 report we take some time to look at a company from Cambridge, Ma. called Foundation Medicine. This cancer genomics play has been pivotal to the mainstreaming of personalised cancer medicine through a product called FoundationOne. Launched in 2012 FoundationOne was the world's first fully informative cancer genomic profile that was 'pan cancer'. By 2017 Foundation Medicine was registering US$152.9m in revenue, up 31% on 2016, with over 67,000 clinical tests performed during the year. In June 2018 the rapid growth of Foundation Medicine prompted Roche to acquire the part of the company that it did not hold in a transaction that valued the company at US$5.3bn.

FOUNDATION MEDICINE WAS TAKEN OUT FOR MORE THAN US$5.3BN

Roche wagers that Foundation Medicine's tests will be needed by oncologists to guide how they fight tumors that vary by patients, regardless of which firm's drug they choose to use. Cancer is a disease of the genome, and they believe genomic profiling of every patient's tumor at the start of their treatment journey will provide transformative outcomes for the patients. Though, by practice and procedure Roche/Foundation might not be a direct competitor to Invitrocue, by test results it very closely does what IVQ does. Consequently we believe that the Roche/Foundation transaction points to the future upside of companies like Invitrocue and bodes well for future acceptance of Onco-PDO by clinicians and patients.

Background to Invitrocue

Invitrocue is a Singapore-based bioanalytics company with global operations in Australia, Asia and Europe, whose products and services help predict the effect of drugs in human tissue before they are used in people. The company was founded in 2012 as a spin-out from A*STAR, the Singapore government's prestigious Agency for Science, Technology and Research, to commercialise '3D cell culture' technology developed by Professor Hanry Yu and colleagues at A*STAR's Institute of Bioengineering and Nanotechnology. In 2019 Invitrocue has two major businesses – a liver model business and a cancer model business. The liver models are primarily used by pharma companies to analyse the *in vitro* toxicity of drug compounds, while the cancer models are used by physicians to develop a drug regimen suitable for individual patients.

What is Invitrocue's field of 3D cell culture and why is the company's technology potentially valuable? Traditionally, when clinicians and research scientists want to study human tissue, they first culture the relevant cells in a lab plate. This results in a so-called '2D cell culture' where the cells spread out in two dimensions. While valuable, 2D cell culture has drawbacks in that cells generally interact with each other in three dimensions, meaning that 2D cell culture models do not accurately reflect all aspects of the tissue as it naturally occurs. Hanry Yu and colleagues have created two distinct '3D cell culture' systems that can overcome many of the traditional drawbacks of 2D systems. For its 3D liver model, Invitrocue's technology is valuable because it provides a better model to study the potential toxicity profile of drugs. For its 3D cancer models, which it calls Onco-PDOs, the value

lies in the ability to run biological simulations that help determine what drugs or drug combinations actually work for individual cancer patients.

Why are Invitrocue's liver models important? One of the more important functions performed by the liver is filtration of the blood to remove toxins. Consequently, before a drug can enter clinical studies ahead of gaining marketing authorisation or regulatory approval, its developers need to assure that it will not be hepatoxic, that is, damaging to the liver. Invitrocue's 3D liver model provides an early way of being able to predict a drug's hepatoxicity profile. For the company, the model provided an initial product with which to start up, and continues to be a core business.

Why are Invitrocue's cancer models important? The striking thing about cancer is its heterogeneity. The baffling variety of gene mutants involved in any one cancer means that every tumour is slightly different. This means, in turn, that different drugs and drug combinations will work for different patients. The ability of Invitrocue's Onco-PDO cancer platform to replicate a patient's own cancer in the laboratory for the purpose of running various drug dosing simulations models and predicting treatment response, opens up a cost-effective way of providing such 'personalised medicine'. Invitrocue screened its first commercial customer in Singapore in April 2018.

INVITROCUE'S ONCO-PDO BUSINESS ALLOWS CANCER TREATMENT PREDICTION

What is the business model for Invitrocue? Invitrocue charges for the reagents and other consumables used in creating its models as well as fees for analysing the data which the models generate. We believe the global market opportunity for the 3D liver model is worth at least US$500m while for Onco-PDO the opportunity is a multi-billion dollar one.

If Invitrocue is so good, why is it capitalised at only A$38m/US$27.5m? Invitrocue is relatively new as a public company, having only listed on ASX in early 2016[3]. We think the story has yet to be widely publicised to investors, in part because the company is based in Singapore whereas its investor based is mostly in Australia. We also think that as knowledge spreads of the bioanalytic power of Invitrocue's models, and as revenue for the business grows, Invitrocue stock will be well-placed to re-rate. We believe that Invitrocue can serve as a 'poster child' for Singapore's vibrant biotechnology sector, which is one of the most productive in the world[4] but is not represented by many publicly traded companies.

Ten reasons to look at Invitrocue

1) **Onco-PDO is a powerful tool for personalised medicine in cancer.** With recently-published data suggesting that patient-derived organoids can be as effective as patient-derived xenografts in selecting drugs specific for a tumour, we believe that Invitrocue is well placed to become a world leader in the field of personalised medicine in cancer through Onco-PDO.

[3] Via a backdoor listing into a shell that was previously called Bunuru Corporation, ASX BUN. Bunuru announced the acquisition of Invitrocue in June 2015.
[4] The Singapore government has also chosen to invest heavily in Life Sciences infrastructure such as the Biopolis science park and various new research centres. It has also used the tax system to encourage Big Pharma to move to the City-State. The government funds basic research heavily through A*STAR.

2) **Personalised medicine in cancer is a large market opportunity**. With ~US$120bn spent annually on drugs to treat cancer, we believe there is at least aUS$2bn market opportunity awaiting any tool that can help tailor the right drugs to the right patients.

3) **Clinical data is coming for Onco-PDO**. Invitrocue has published two milestones scientific papers in the prestigious journals *Nature Medicine*[5] and *Nature Communications*[6] using more than 200 laboratory and clinical data points. More clinical partnerships are being set up globally in all key cancer indications and markets, including Australia, Singapore, Hong Kong, Japan, Germany and the UK. More recently, the company published another two peer-reviewed papers describing its ability to build *in vitro* lung cancer and liver cancer organoids.

4) **Commercial readiness.** The company is in the process of setting up a global network of Onco-PDO joint laboratories with key leading scientific and clinical thought leaders. This approach will not only fast track its clinical validation but build a ready channel for commercialisation. Invitrocue received its first commercial patients in 2018.

INVITROCUE RECEIVED ITS FIRST COMMERCIAL PATIENTS IN 2018

5) **The regulatory hurdles are low for Onco-PDO**. Since Onco-PDO is, in effect, a biological decision support system to guide the on-label use of approved drugs, there is no immediate need to seek regulatory approval before marketing the product. This makes it relatively easy for Invitrocue to grow early revenue, Obviously, once the product transitions to a kit-based form, a mere 510(k) approval in the US market would be all that is required, and achievement of this clearance plus a CE Mark can then take the business to the next level.

6) **HepatoCue provides better tools for evaluating liver tox**. The ability to better understand the hepatotoxicity profile of a drug is worth >US$500m, a market which Invitrocue is well placed to go after with HepatoCue.

7) **The rise of liver disease is increasing the value of HepatoCue as a diagnostic tool**. With Hepatitis B and NASH, among other conditions, representing a heavy disease burden, Invitrocue's 3D liver models may potentially be used to screen for novel drug compounds in what is an important and potentially lucrative area of unmet medical need.

8) **Invitrocue is growing sales**. The revenue base, while small (ie only S$0.8m in calendar 2017 and S$0.7m in calendar 2018), is set to growing quickly due to the relative ease with which Invitrocue can gain early commercial users from its foundation technologies.

9) **Invitrocue has a solid management team**. CEO Dr Steven Fang previously built Cordlife, a successful Singapore-based cord blood bank. Backing Fang is a quality board that includes founder Professor Hanry Yu.

10) **Invitrocue has upside on our numbers.** We value Invitrocue at 7.3 cents base case and 24.4 cents per share optimistic case. Our target price of 16 cents per share sits at the midpoint of our valuation range. For the assumptions that went into our valuation see our 20 April 2018 note headlined 'The next step in predicting cancer treatment outcomes'.

[5] Nat Med. 2017 Oct;23(10):1167-1175. Epub 2017 Sep 18.
[6] Nat Commun. 2017 Sep 5;8(1):435.

Risks related to Invitrocue

Risks specific to Invitrocue. We see five major risks for Invitrocue as a company and as a listed stock:

- **Market acceptance**. There is the risk that Onco-PDO will fail to attract a strong following from oncologists.
- **Funding risk**. More capital will likely be needed to continue clinical and commercial development of Onco-PDO as well as Invitrocue's other projects in the bioanalytics field.
- **Regulatory risk**. There is the risk that Invitrocue may be required to develop more data on the clinical effectiveness of Invitrocue before it is permitted to offer Onco-PDO services in major markets.
- **Distribution risk.** There is the risk that Invitrocue will fail to find commercial partners allowing it to build a global reach with its current suite of services.
- **Technology risk.** There is the risk that newer technologies with a superior cost profile in the personalised oncology space can emerge before Invitrocue has fully realised the commercial potential of Onco-PDO.

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

- The stocks of biotechnology and medical device companies without revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character.
- Since most biotechnology and medical device companies listed on the Australian Securities Exchange fit this description, the term 'speculative' can reasonably be applied to the entire sector.
- The fact that the intellectual property base of most biotechnology and medical device lies in science not generally regarded as accessible to the layman adds further to the riskiness with which the sector ought to be regarded.

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

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