PITT STREET RESEARCH

Imagion Biosystems

Novel cancer diagnostics with de-risked commercialisation

Share Price: A$0.016

Imagion Biosystems (ASX:IBX) is an Australian medical technology company developing the MagSense diagnostic imaging technology. MagSense can potentially improve on positron emission tomography (PET) and conventional magnetic resonance imaging (MRI) imaging modalities.

ASX:IBX

Sector: Health Care Equipment & Services

12 April 2023

MagSense is a game changer in cancer diagnostic imaging

MagSense is an important improvement in the standard of care and could allow for highly sensitive, specific and safe detection of certain cancers at a much earlier stage. Imagion is currently in phase 1 trial (in-human study) of MagSense for HER2-positive breast cancer, and in pre-clinical stages for diagnosis of prostate, ovarian and brain cancers. The market opportunity for HER2-positive breast cancer alone is significant given that MagSense can eliminate lymphadenectomy in possibly 50% of the patients and remove uncertainties related to mammograms.

An accelerated commercialisation path awaits

In February 2023, Imagion received encouraging feedback on MagSense technology from an independent panel of breast cancer radiologists, which highlighted the potential use of its imaging agent for detection of tumour cells in lymph nodes by an MRI scanner. Thereafter, Imagion decided to prioritise the use of its MagSense imaging agent with the large installed base of MRI sites to accelerate commercialisation, which markedly increases the overall opportunity. Moreover, Imagion recently received positive feedback from the FDA in relation to its proposed phase 2 design for its HER2 imaging agent. The company is now planning a multi-site phase 2 clinical trial in the US and hopes to file an Investigational New Drug (IND) application in Q4 2023 or Q1 2024.

Imagion is undervalued based on our estimates

We value Imagion at $83.1m in our base case and $126.7m in our optimistic case using a DCF approach. This equates to 3.6c per share and 5.5c per share respectively taking into account anticipated dilution in the next few years. At the current number of shares, however, this is 7.3c per share base case and 11.2c per share bull case. We believe investors are not fully factoring in the company's unique technology proposition, huge addressable market and recent steps to de-risk its commercialisation process. Please refer to page 18 for the key risks.

Market cap. (A$m)	17.9
# shares outstanding (m)	1,121.0
# share fully diluted	1,411.0
Market cap ful. Dil. (A$m)	22.6
Free float	100%
12 months high/low (A$)	0.058 / 0.014
Average daily volume (x1,000)	1,987.1
Website	www.imagionbiosystems.com

Source: Company, Pitt Street Research

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

Source: Refinitiv Eikon, Pitt Street Research

Valuation metrics	
DCF valuation range (A$)	0.036-0.055
WACC	10.6%
Terminal growth rate	2%

Source: Pitt Street Research

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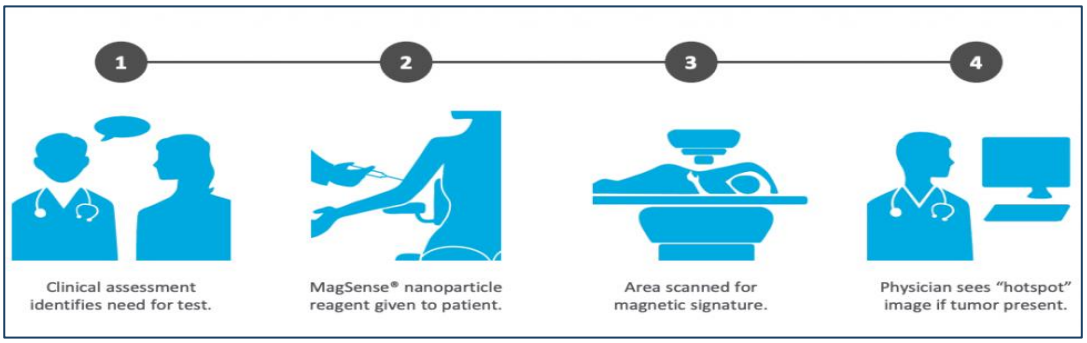
Introducing Imagion Biosystems

Who is Imagion Biosystems (ASX:IBX)? Is a diagnostic imaging technology developer. Imagion Biosystems (Imagion) is an Australian diagnostic imaging technology developer. The company's MagSense diagnostic imaging technology, is detectable by MRI scanners, and can potentially improve on other imaging modalities Imagion also sells superparamagnetic iron oxide particles, branded as PrecisionMRX suited for biomedical applications. The FDA granted MagSense a Breakthrough Device designation in July 2019 as part of the Company's plan to develop a proprietary detection platform. The company is targeting to use its technology for diagnosing multiple oncology indications including HER2 breast cancer, prostate cancer, ovarian cancer and brain cancer.

Imagion's MagSense imaging agent is expected to be used in tumour detection by mainstream MRI systems

Imagion presented phase 1 interim data for its MagSense HER2 breast cancer imaging agent at the San Antonio Breast Cancer Symposium in December 2022. The company has decided to focus on using its MagSense nanoparticle imaging agents in conjunction with available MRI technology (Figure 1). This strategy will likely provide Imagion access to a wider immediate addressable market on the back of large installed base of existing MRI facilities, globally. We believe, by using MagSense imaging agent in the conventional MRI workflow, Imagion will accelerate its commercialisation strategy. The company estimates the price of each cancer test for monitoring/staging HER2-positive breast cancer to be US$1,500, at an attractive ~80% gross margin.

Figure 1: MagSense's working model



Source: Company

Imagion's MagSense technology is highly accurate, safe and accessible. The MagSense technology is potentially better than other imaging modalities such as PET or non-targeted MRI as it does not involve ionizing radiation, radioactive tracers and does not provide specific detection of the cancer for non-targeted MRI. The technology uses magnetizable iron oxide nanoparticles conjugated to target-specific molecules, such as antibodies where the nanoparticles can be detected using readily available magnetic resonance imaging protocols.

MagSense works as a superior imaging tool because the magnetic property of the bio-safe nanoparticles allows the MRI scanner to detect the nanoparticles with an image pattern that is distinct when the antibody has bound the nanoparticles to its target. Imagion believes that the MagSense technology is more sensitive than CT scans[1], with tumours smaller than one centimeter potentially able to be detected. The integration of the MagSense

[1] That is, MagSense has a detection threshold of less than 1 million cells.

imaging agent into mainstream clinical MRI scanners as a part of a standard diagnostic procedure makes the technology more accessible to the health care ecosystem. MagSense also demonstrates the potential of eliminating the standard invasive biopsy procedures.

Imagion is already in the clinic for HER2-positive breast cancer, and in preclinical stage for prostate and ovarian cancers

MagSense's robust product pipeline. In May 2021, Imagion undertook a first-in-human study of the MagSense technology in HER2-positive breast cancer (targeting HER2 expression). In December 2022, at the San Antonio Breast Cancer Symposium, the interim data for phase 1 clinical study in HER2-positive breast cancer was presented. The goal was to establish a non-invasive method for the detection of lymph nodes cancer (as compared to conventional biopsy of the sentinel lymph nodes). In February 2023, Imagion received positive feedback on MagSense technology from an independent review conducted by a panel of expert breast cancer radiologists, stating that MagSense imaging agent could be potentially used for detecting tumour cells in lymph nodes by using an MRI scanner. Thus, the company now prioritises the use of MagSense imaging agent (rather than the physical device) with the available mainstream MRI workflow while integrating into the standard clinical protocols of diagnosis and imaging. Besides breast cancer, MagSense is under preclinical development for its application in diagnosis of prostate and ovarian cancers. The technology is also being researched in brain cancer diagnosis under product concept stage. Further, Imagion is exploring the use of its nanoparticles as a vascular imaging aid in the diagnosis of cardiovascular diseases.

Imagion is undervalued due to lingering investor sentiment. We believe Imagion's market value is not a true reflection of the intrinsic value of the stock. We think the main problem has been poor investor sentiment due to past delays – in particular the delay in completing the Phase 1 study. However, investors are not fully factoring in positive data reported and recent steps to de-risk the commercialisation process as well as the company's unique position in the market and its huge addressable market. Furthermore, the company has been successful in arranging growth funding in this year amidst tight market conditions and this is a reflection of the strength of its business proposition. We see Imagion re-rating as the technology moves further into clinic and shows encouraging results for different cancer types.

Ten reasons to look at Imagion

1) **MagSense is an important improvement in the standard of care.** It allows for sensitive, specific and safe detection of cancer at a much earlier stage of development than competing modalities such as ultrasound, CT and conventional non-targeted MRI scans.

Imagion is aiming to file an IND submission by Q4 2023/Q1 2024

2) **MagSense's HER2 imaging agent will be a part of the current standard cancer diagnosis protocol.** This is because the agent can detect tumour cells in lymph nodes through conventional MRI scanners. This finding is in line with the positive outcome of an independent review announced in February 2023. The blinded review was undertaken by a panel of radiologists who confirmed that MagSense's HER2 imaging agent produced a distinct image pattern in nodes highly suggestive of tumour as compared to the contrast found in non-involved nodes. Imagion will now focus on using the MagSense imaging agent in conjunction with a large installed base of MRI sites to accelerate commercialisation, which markedly increases the market opportunity.

3) **Imagion announced in March 2023 that it has received positive feedback from FDA in relation to its proposed phase 2 design for its HER2 imaging agent.** The company plans to proceed with a multi-site phase 2 clinical trial in the US based on this design. It is expected that it will file an IND application in Q4 2023 or Q1 2024. This provides investors with a clear sense of direction in the next 12 months and (if granted) potential upside.
4) **The business opportunity for Imagion with MagSense is large,** given that the HER2, Prostate and Overian cancer markets (the key markets for Imagion) are ~$5bn. The broader cancer diagnostic tools represent a US$100bn market globally and the largest share of that market represents diagnostic imaging.
5) **The market opportunity for diagnostic and treatment tools for HER2-positive breast cancer is particularly significant** since the use of MagSense can eliminate lymphadenectomy in possibly 50% of the patients and improve on the uncertainties with conventional imaging. There are ~50,000 new cases of HER2-positive breast cancer in the US annually.
6) **MagSense has a strong product pipeline with the working to target different oncology indications**. In 2021-2022, Imagion advanced its clinical study in brain cancer by collaborating with Patrys, a Sydney-based biotech company, while in prostate cancer, Imagion has received two CSIRO grants and presented the preclinical research data at World Molecular Imaging Congress (WMIC). Currently, the ovarian cancer preclinical development is also in progress. In addition, Imagion intends to explore the use of MagSense as a vascular imaging aid for the diagnosis of cardiovascular diseases.

MagSense has the potential to be used for multiple indications with high unmet needs

7) **In 2022 Imagion expanded its US operations and R&D facility in San Diego to bolster internal nanoparticle research and development capabilities**. Moreover, with the new facility the company is ready to leverage the additional manufacturing capacity to support clinical programmes and generate revenue through third-party commercial relationships.
8) **Imagion has a strong leadership team. Robert Proulx** is Imagion's CEO and VP and has more than 25 years of experience in the field of life sciences and medical diagnostics. Imagion's Chief Development Officer is **Dr. Yalia Jayalakshmi**, who holds 25 years of biopharmaceutical and interoperative optical imaging experience. Further, **Dr. Marie Zhang,** the VP of R&D, has worked with various biotech companies over the last 25 years including preclinical drug development. The directors of Imagion are **Mike Harsh** (a long-time head of diagnostic imaging engineering at GE), **Dianne Angus** (a senior biotech and healthcare executive and IP lawyer), **David Ludvigson** (a US life sciences and diagnostics entrepreneur), **Jovanka Naumoska** (an Australian corporate lawyer) and **Mark Van Asten** (an Australian diagnostic entrepreneur).
9) **The company has recently closed a funding commitment of ~A$18m.** In March 2023, Imagion announced that it will raise up to A$2.4m through an entitlement offer to existing eligible shareholders. The company has also received a commitment of up to A$15m funding from Mercer Street Capital Partners LLC. These funds will be used to prepare the MagSense HER2 breast cancer imaging agent for the next phase of clinical development as well as to grow the pipeline in other oncology indications.

10) **We believe Imagion is undervalued.** We value Imagion at $83.1m in our base case and $126.7m in our optimistic case, using a DCF methodology. Accounting for future dilution, this equates to 3.6c per share and 5.5c per share respectively. Based on the current number of shares on issue, the company is worth 7.2c per share base case and 11.3c per share bull case. We think the stock will re-rate towards our valuation range as MagSense moves further into clinic, meets its commercialisation milestones and exhibits encouraging clinical results for various cancer types.

MagSense is bridging the gap between traditional imaging and newer screening technologies

The technology is being developed to provide a high-level overview of cancer cells.

The MagSense technology is being developed with the objective of bridging the gap between existing medical imaging technologies, which lack the ability to identify the molecular makeup of the region of interest, and newer screening technologies - such as liquid biopsy - that come with limited ability to precisely locate diseased tissue. The technology is being developed to provide a high-level overview of cancer cells – including (but not limited to) information such as location of tumour, size of tumour and details such as molecular specificity. Currently, the MagSense technology is being investigated for the detection and diagnosis of solid cancerous cells, such as those present in breasts, prostate or ovaries. We believe this technology can be further expanded to other indications once the proof-of-concept is established.

MagSense's development story

Dr. Edward Flynn, a nuclear physicist, who until the late 1990s was a researcher at Los Alamos National Laboratory, originally developed the MagSense technology. In the late 1990s, Dr Flynn founded a company called Senior Scientific to take the development of MagSense technology ahead. The company, in 2011, was acquired by New York-based Manhattan Scientifics. In 2016, Imagion Biosystems was formed to acquire the MagSense project from Manhattan Scientifics, and the company operations were moved from Albuquerque, New Mexico, to San Diego, California. Imagion Biosystems went public on the ASX in June 2017 after raising A$12m at 20 cents per share.

During 2017 and 2018, Imagion worked on further developing the technology from the basic proof-of-principle to a state of readiness for moving into clinical testing. By September 2018, Imagion had initiated manufacturing of the first batch of nanoparticles as per GMP standards, which was needed for clinical testing. Imagion commenced pre-clinical safety and toxicology studies for its lead indication in February 2019. Notably, the FDA granted MagSense the Breakthrough Device designation in July 2019. Although this is less relevant now considering the transition to using MagSense as an imaging agent, this achievement cannot be forgotten - it help its cause when it eventually seeks FDA approval given it will be familiar with the technology.

In H1 2021, Imagion started the enrollment for phase 1 trial for MagSense technology for detecting HER2 metastatic breast cancer started. In December 2022, the company presented the interim results of its phase 1 study at the San Antonio Breast Cancer Symposium, highlighting the specificity and safety of MagSense® and in February 2023 announced the strategic shift to use of MRI as the detection method. Most recently, in March 2023, Imagion received positive feedback from FDA in relation to its proposed phase 2 trial design, based on which the company is planning to conduct a multi-site phase 2 clinical trial in the US. Imagion envisages filing the IND submission by Q4 2023 or Q1 2024.

How MagSense works

The MagSense technology delivers nanoparticles loaded with antibodies specific to target cells to diagnose diseases.

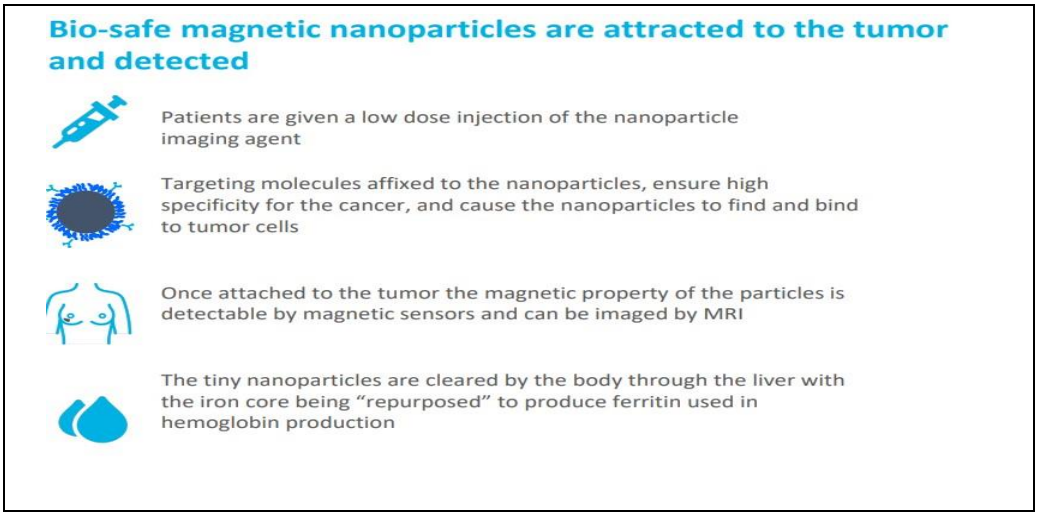
The MagSense technology uses the unique properties of specialised nanoparticles to detect diseased areas, such as cancer, present in the human body based on their distinct cell features. These nanoparticles are conjugated with targeting molecules, such as antibodies or small molecules to enable them to bind with specific antigens present on the surface of the target cells.

Upon binding, the nanoparticles are detectable by their magnetic signature, which is not exhibited by any other structure in the human body.

The detection of magnetic nanoparticles in an MRI scan allows the radiologist to determine if cancer cells are present. This is a vast improvement over current imaging which focuses on identifying anatomical or morphological irregularities in the scan area. Furthermore, the physics and principles of detecting iron oxide nanoparticles by MRI are already well characterised by and described within the research and clinical community, which means the method being employed by the company for detecting different types of tumours, including prostate, ovarian or breast tumour cells would be more likely to be adopted.

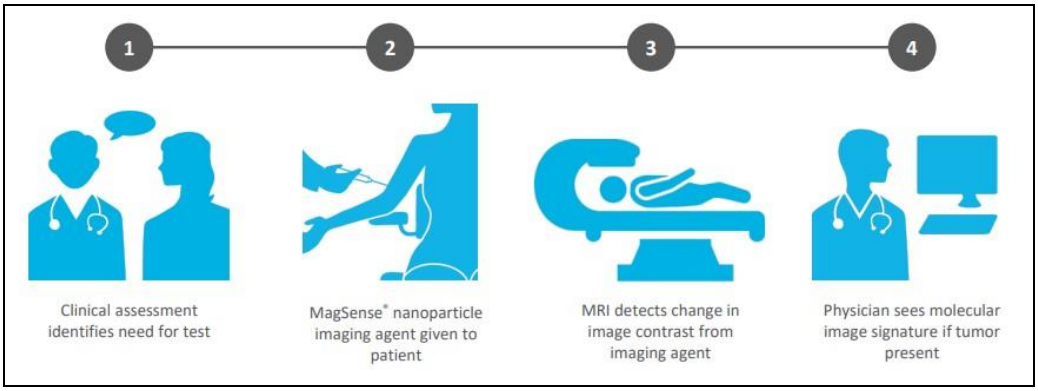
A typical MagSense procedure (Figures 2 and 3) will involve the administration of a small intravenous injection (or injection via another route of administration) of cancer-specific targeting nanoparticles to patients followed by an MRI scan the same day (or next day). The MRI scan will reveal a distinct pattern if cancer cells are present. When combined with conventional information such as irregular tissue morphology, the image contrast created by MagSense® imaging agent provides added context for the radiological review.

Figure 2: How MagSense works



Source: Company

Figure 3: MagSense' use in the context of its use

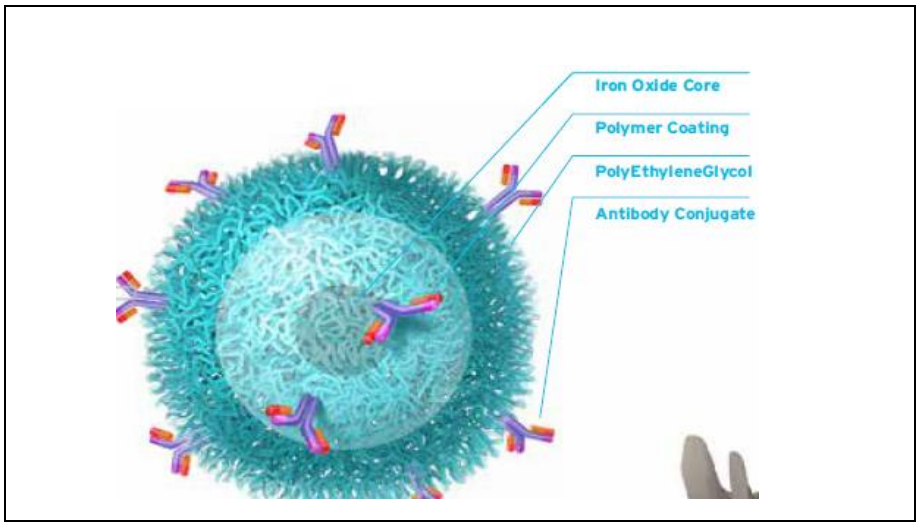


Source: Company

Specialised and distinct nanoparticles are prepared for each tumour cell-type

Considering that there is no 'pan cancer' biomarker available, in order to detect or quantify different types of cancers, distinct formulations of target nanoparticles are required – specific to antigens presented by each tumour cell-type. MagSense nanoparticles will be an injectable solution of uniformly formed superparamagnetic 25 nm magnetite (Fe_3O_4) nanoparticles, which Imagion sells for research and commercial use as PrecisionMRX nanoparticles. The particles have a protective coating of polymer which provides the ability to make it bio-functional. Polyethylene glycol is added to the nanoparticles to make them 'stealth' to a body's immune system – allowing them to remain in circulation for a long time (Figure 4). Additionally, a specific antibody or ligand is conjugated to the nanoparticles to allow the latter to bind with target cells.

Figure 4: MagSense nanoparticles



Source: Company

These nanoparticles will be synthesised using a proprietary method that will allow them to be manufactured with an extremely narrow tolerance of core particle size, shape and magnetic properties, and will provide high detection sensitivity. Post synthesis of the nanoparticles, the formulation will be packaged and supplied to customers by Imagion as a single-use vial/pre-packaged syringe. For each type of cancer test, an optimum dose or volume of nanoparticles will have to be determined during clinical studies. Based on human studies, Imagion has found that nanoparticle volumes administered to patients have a wide tolerance and are safe.

Imagion is the first company to show that targeted NPs are achievable.

Imagion is the first company to show that targeted NPs are achievable. Previous efforts have all been with general purpose (non-targeted agents like gadolinium or iron oxide) but never achieved the specificity. The company has a first of its kind product. It has shown that it can make these targeted particles to target different types of tumors, e.g prostate, ovarian. When we first covered this company in 2019, the company had ambitions to do this, but now has realised them.

MagSense is superior to other imaging modalities

Currently, several procedures are available for diagnosing breast cancer and its stage. This typically involves the use of mammography, conventional non-targeted MRI or ultrasound and lymph node biopsy – the latter being the definitive means of diagnosing and determining the stage of breast cancer. However, these procedures are neither economical nor safe (invasive in nature) for patients, as they require the collection of the target tissue to carry out diagnostic operations. There is a significant unmet need for diagnostic systems that can monitor as well as quantify disease progression in an economical and non-invasive manner. We think that MagSense tests are likely to emerge as an ideal diagnostic modality for the monitoring of breast cancer disease progression.

MagSense's HER2 imaging agent de-risks and accelerates the commercialisation path

As part of Imagion's market entry strategy, its initial aim was to commercialise its proprietary technology for monitoring the progression and staging[2] of HER2-positive breast cancer, which is one of the most prominent types of cancer. The HER2 subtype of breast cancer is an aggressive phenotype demonstrating high chances of recurrence and metastasis. Every year, HER2-positive breast cancer accounts for almost 15–20% of the ~2.3 million breast cancer patients globally. This translates to 345,000–460,000 patients with HER2-positive breast cancer every year. The high patient population represents a significant addressable market for diagnostics companies such as Imagion.

Use of MagSense imaging agent with existing MRI systems for detecting HER2-positive breast cancer will accelerate Imagion's market access

Imagion presented its phase 1 interim data for its MagSense HER2 breast cancer imaging agent at the San Antonio Breast Cancer Symposium, in December 2022. The interim data had no safety or adverse events reported related to the imaging agent in patients. In February 2023, Imagion received a positive outcome on MagSense technology through an independent blinded review conducted by a panel of expert breast cancer radiologists. The radiologists confirmed that the MagSense HER2 imaging agent can detect tumour cells in lymph nodes by MRI scanners. While reviewing the scan, the contrast created by MagSense in lymph nodes indicated the presence of tumour cells that was significantly different from the contrast viewed in non-involved nodes. **In light of this, the company plans to prioritise MagSense's use in existing clinical workflows with conventional MRI machines.** We know that the existing base of installed MRI facilities globally is large[3]. The use of MagSense HER2 imaging agent for nodal assessment of breast cancer results in a total addressable market of US$337m (A$500m) annually. The company estimates the price of each cancer test for monitoring/staging HER2-positive breast cancer to be US$1,500 (at an ~80% gross margin). We believe, the company's decision to use MagSense HER2 imaging agent with MRI machines will accelerate the path to commercialisation and eliminate technical risks.

Furthermore, in March 2023, Imagion released an update that it has received encouraging feedback from the FDA in relation to its proposed phase 2 trial design. The FDA has provided further guidance and suggestions outlining the regulatory oversight for initiating phase 2 trials. Imagion plans to proceed with a multi-site phase 2 clinical trial in the US. This study will evaluate different clinical endpoints and help optimise dose and imaging parameters,

[2] Progression refers to expansion in the size of individual tumours. Staging refers to the level of spread of the cancer through the body.
[3] https://www.statista.com/statistics/282401/density-of-magnetic-resonance-imaging-units-by-country

while setting the ground for a phase 3 pivotal investigation. Imagion is likely to file the IND submission in Q4 2023 or Q1 2024.

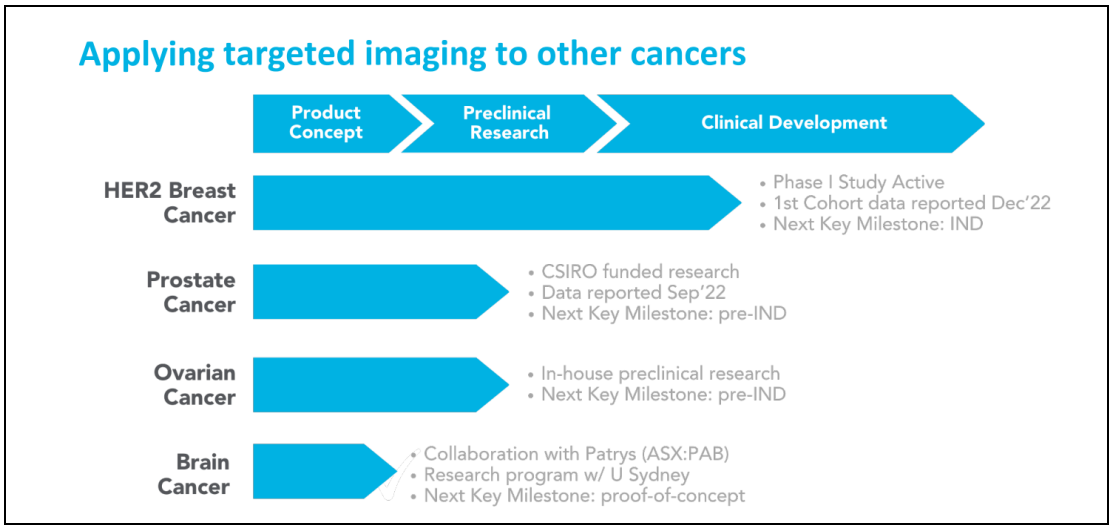
Based on the FDA guidance, Imagion is preparing for the following activities:

- Gathering additional clinical and non-clinical data to support the initiation of the US phase 2 study.
- Manufacturing the required MagSense HER2 imaging agent material to conduct the phase 2 study.
- Deciding on initial clinical investigators and sites to perform the phase 2 study.

Expansion of MagSense technology across other cancer types with a high unmet medical need

Apart from HER2-positive breast cancer, Imagion is extending the use of MagSense to other types of cancers such as prostate cancer, ovarian cancer and brain cancer (Figure 5).

Figure 5: MagSense product pipeline



Source: Company

The company advanced its preclinical prostate cancer research and in September 2022, it presented a poster at the WMIC stating that MagSense molecular imaging agent showed high specificity and selectivity for both MRI and its proprietary Magnetic Relaxometry Imaging (MRX). Imagion received two grants to support its preclinical research for prostate cancer – in 2021, the company received the first grant of A$50,000 under the Entrepreneurs' Programme of the Australian Government Department of Industry, Science, Energy and Resources, while in March 2023, the company was qualified for another grant of A$50,000, under the same programme of the Australian Government Department of Industry, Science, Energy and Resources.

In May 2021, Imagion collaborated with Patrys Limited (a Sydney-based company focussed on developing novel antibody technology to detect cancer) to understand the use of Patrys' PAT-DX1 deoxymab antibody[4] with MagSense nanoparticles to improve brain tumour imaging and diagnosis with the highly specific imaging agent. Further, the use of MagSense for ovarian

[4] PAT-DX1 deoxymab antibody is a humanised form of antibody used for human therapeutic applications.

cancer diagnosis is under preclinical development, which is being conducted in-house by Imagion. In addition to this, in April 2022, Imagion entered into a research agreement with Massachusetts General Hospital to explore the use of iron oxide nanoparticles for vascular imaging in diagnosis and treatment of certain cardiovascular diseases.

Towards the beginning of 2022, Imagion inaugurated a new R&D facility in San Diego, US, to expand the internal nanoparticle research and development capabilities. This facility is going to offer additional manufacturing capacity for supporting clinical programmes as well as help generate revenue via third-party commercial engagements.

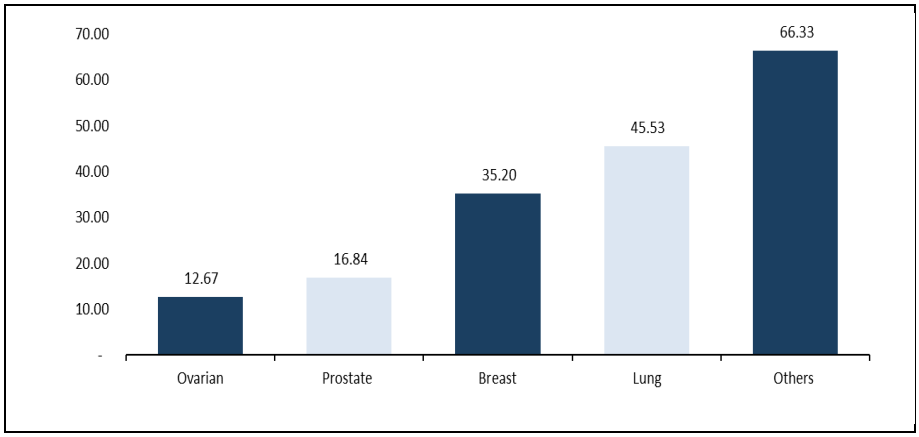
Clinical development of MagSense for diagnosis of multiple cancers is expected to unlock multiples revenue streams in future

The MagSense product pipeline is set to tap major markets of cancer diagnostics

Lucrative cancer diagnostics market creates a tailwind for Imagion's MagSense technology

With the potential application of MagSense technology across multiple cancer types, Imagion will be able to access the promising market of cancer diagnostics, which is likely to reach US$336bn by 2031, according to Transparency Market Research. The market is expected to grow at a CAGR of 7.4% over 2022-2031. Imagion aims to commercialise its technology for breast, prostate, ovarian and brain cancers. Apart from this, Imagion is exploring the possible use of MagSense for the diagnosis and treatment of certain cardiovascular diseases. Estimates suggest that by 2022, global annual spending on the diagnosis of breast cancer, prostate cancer and ovarian cancer is likely to exceed US$35bn, US$17bn and US$13bn, respectively (Figure 6). According to the World Health Organization, cancer caused ~10 million deaths in 2020. By the end of 2030, new cancer cases will likely rise by ~70%.

Figure 6: US$177bn global cancer diagnostics market[5]



Source: Transparency Market Research and Analysis

Non-invasive and non-radioactive MagSense technology is likely to address high unmet medical needs in cancer diagnosis and imaging.

The rising demand for non-invasive cancer diagnostic procedures from the patient and physician community clearly indicates the significant opportunity for Imagion in the field of cancer diagnostics. Within cancer diagnostics spending, imaging tests (such as MRI, CT, mammography) capture the major share of global spending, whereas biopsy- and biomarker-based diagnostics account for a small proportion of the total global spend. Despite being widely

[5] Others comprise blood, pancreatic, kidney, brain, colorectal and liver cancers.

adopted by new cancer patients, imaging procedures are not capable of diagnosing and quantifying diseases in the initial stages of cancer progression. Coming to surgical and biopsy procedures, we see there is a need to reduce these invasive approaches for detecting cancers during the early stages of the disease.

Thus, in our view, there is a major need for a non-invasive and non-radioactive diagnostic methods that will help reduce chances of metastases. Imagion's MagSense is likely to be a game changing solution addressing this unmet need because it can be used as an effective imaging agent with conventional MRI scanners in existing clinical practices. Thus, MagSense clearly offers an edge over currently deployed diagnostic procedures.

Breast cancer – the priority indication for commercialisation

Imagion is currently focussed on commercialising its technology for improving the survival prospects of patients with breast cancer, which represents the second leading cause of cancer deaths among US women, according to the American Cancer Society. On average, one woman is diagnosed with breast cancer every two minutes, and one woman is expected to die due to breast cancer every 13 minutes. In 2022, according to the American Cancer Society, an estimated 287,850 new cases of invasive breast cancer were diagnosed in women, in the US, along with 51,400 new cases of non-invasive breast cancer. The rising burden of breast cancer among women is alarming, presenting a significant addressable opportunity for providers of cancer diagnostic tools and platforms. We believe that MagSense has the potential to capture a major portion of the overall breast cancer diagnostics market, given its positive results from recently conducted research studies.

Currently, mammograms[6] are typically used for the screening or detection of breast cancers. According to MQSA National Statistics by FDA, each year, over 39.5 million mammograms are performed in the US (as of January 2023), translating into annual spending of over US$10bn. Further, of the total 39.5 million patients, about 50% of women experience false-positive results at least once during a period of 10 years while undergoing annual mammography procedures. Hence, they are required to undergo a lymph node biopsy to confirm the diagnosis. Additionally, breast cancer is often detected at later stages because mammograms are unable to detect the cancer when it is still in the initial stage. Between 2017 and 2030, the worldwide breast cancer mortality is projected to rise ~12.4%. Imagion's technology presents a solution to this challenge by allowing early detection and continuous monitoring of disease progression. The technology is currently in phase 1 showing encouraging results.

Prostate cancer – a medium-term opportunity for Imagion

Prostate cancer, which represents the second most common cause of death among men (according to the American Cancer Society), is another type of cancer being targeted by Imagion's MagSense. Prostate cancer, which is diagnosed in about one in eight men during their lifetime, results in one death every 15 minutes. According to ZEROCANCER 2023 estimates, the disease is likely to affect 288,300 new men in the US – representing a large patient population that can be captured by the diagnostic test being developed by Imagion.

[6] Mammogram is an X-ray picture of the breast, which is captured to check for breast cancer in women.

Imagion progresses its preclinical research for prostate cancer, the second most common cause of deaths in men

Currently, a prostate biopsy is the most common procedure for the diagnosis of the disease[7] – however, in some markets such as Australia, the standard is PSMA PET imaging. In the US alone, annual spending of US$5.5bn to US$8.2bn is incurred to detect, screen and diagnose prostate cancer. In the US there are ~14,000 MRI machines with ~2,500 PET machines. However, despite the huge spending, the disease metastasises in 28% of the cases[8]. Therefore, there is a need for a screening-cum-diagnostic tool that is more accurate and affordable for the diagnosis of life-threatening prostate cancer. We believe the MagSense technology has the potential to address these needs in the medium term. In markets where medical practice has already dropped biopsy, MagSense will be competing with a bio-safe and non-radioactive approach. However, we believe the technology has a competitive advantage, including cost. MagSense is currently under preclinical development for use in prostate cancer patients. This imaging tool presented in WMIC is considered highly specific and selective for both MRI and MRX.

Ovarian cancer – another indication targeted by Imagion

Ovarian cancer is another indication being targeted by Imagion. The disease is likely to affect almost 19,710 US women and kill approximately 13,270 among them as per 2023 estimates by the American Cancer Society. Unlike breast cancer, which can still be detected in early stages via screening tools, only 20% of ovarian cancer cases are detected in early stages. This leads to a severe decline in the survival prospects of patients with ovarian cancer, which stands at 92% if detected early and 27% if detected post metastases. Imagion's MagSense technology has the potential to target this unmet medical need for procedures/screening tools that could possibly detect ovarian cancer at earlier stages, thereby increasing the survival prospects of patients. It is currently under preclinical development for use in the diagnosis of ovarian cancer.

As of now, the commonly used tests for ovarian cancer screening are transvaginal ultrasound (TVUS) and the CA-125 blood test; however, these tests have limited diagnostic performance for the detection of diseases in their early stages. As Imagion is expected to price the MagSense product for ovarian cancer at US$1,500 per test, upon global commercialisation, the product has the potential to generate ~US$29.6m in revenue from the US market alone, assuming all new ovarian cancer cases (~19,710) in the US adopt Imagion's technology.

Brain cancer – a potential area of investment for Imagion

Imagion is exploring the use of MagSense nanoparticles to advance brain tumour imaging and diagnosis

Brain cancer is the tenth leading cause of death for men and women. According to the Data Bridge Market Research, the global brain cancer diagnostic market is expected to grow at a CAGR of 18.9% over 2023-2030. This high-growth market is also being targeted by MagSense. Imagion collaborated with Patrys Limited to understand the use of Patrys' PAT-DX1 deoxymabs antibody with MagSense nanoparticles to improve brain tumour imaging and diagnosis. We believe this highly specific diagnosis will enable early detection of brain cancer, thereby increasing the five years survival rate for brain cancer.

In 2023, it is estimated that 24,810 adults will be diagnosed with primary cancerous tumours of the brain and spinal cord in the US, as per Cancer.Net.

[7] *Prostate Cancer,* Centre for Disease Control and Prevention, 25 August 2022.
[8] In case the disease is not detected in earlier stages.

Primary tumours of brain and spinal cord typically start from the brain or spinal cord. Brain tumours account for 85-90% of all the primary central nervous system (CNS) tumours. In the US, the five year relative survival rate is 36% for a cancerous brain or CNS tumour. Worldwide data reveals that in 2020, an estimated 251,329 people died due to primary cancerous brain and CNS tumours. We believe that an early diagnosis of tumour is likely to reduce the number of deaths.

A brain tumour diagnosis usually starts with an MRI followed by tissue sampling through biopsy or surgery. Imagion's non-invasive and non-radioactive MagSense is expected to evolve as a promising diagnosis tool for brain cancer. Given the prospective use of MagSense imaging agent in conjunction with conventional MRI scanners, integrating it in the current standard of care diagnosis will be seamless. The other methods of diagnosing brain cancer are CT scan, PET, cerebral arteriogram, lumbar puncture, myelogram, biomarker testing of the tumour, neurological, vision and hearing test, neurocognitive assessment, electroencephalography (EEG) and evoked potentials.

Success in securing growth funding is another critical milestone

In March 2023, Imagion announced a non-renounceable entitlement offer to its shareholders seeking to raise up to A$2.4m as well as a funding facility with Mercer Street Global Opportunity Fund LLC, a US-based investment fund managed by Mercer Street Capital Partners LLC, of up to A$15m. The combined funding is expected to be utilised for multiple purposes including (i) preparing HER2 breast cancer imaging agent for the next phase of clinical development; (ii) pipeline growth into other oncology indications such as prostate and ovarian; and (iii) additional general working capital. We believe this is an important milestone that will facilitate the company's commercialisation plans and provide confidence to investors, particularly in the context of the market volatility.

Imagion secured funding commitments of about A$18m in March 2023

Non-renounceable share offer. Imagion seeks to raise up to A$2.4m through offering non-renounceable one new fully paid ordinary shares in the company for every eight shares held by eligible shareholders registered at 10 March 2023 at an issue price of A$0.017 per share. The maximum number of shares issued will be 140 million.

Funding from Mercer Street Global Opportunity Fund. Imagion can raise funding of up to A$15m in three tranches:

- **Tranche 1 –** Convertible securities with a face value of A$1.65m to be purchased for A$1.5m. Mercer will have the right to convert the notes into fully paid ordinary shares at 90% of the lowest volume weighted average price (VWAP) during the 15 trading days immediately prior to the issue of a conversion notice, subject to a floor price of A$0.0125.
- **Tranche 2 –** The second tranche of convertible securities with a face value of A$1.1m will be purchased for A$1m and entitles Mercer the right to convert the note into fully paid ordinary shares at 90% of the lowest VWAP during the 15 trading days immediately prior to the issue of a conversion notice, subject to a floor price of A$0.0125.
- **Tranche 3 –** Imagion can raise A$12.5m (in multiples of A$0.5m) subject to mutual agreement between Imagion and Mercer. All subsequent drawdowns are subject to the same pricing and other mechanisms as the

first two tranches and all tranches have a term of 18 months from drawdown.

- Mercer has received 20.2 million new shares (representing 2.5% of total facility) at no cost for entering into this agreement at an issue price of A$0.017/share.
- No interest is payable on the unconverted drawn funds. Mercer can have maximum of 9.99% of shareholding in Imagion at any point of time.

Valuing Imagion

We value Imagion at $83.1m in our base case and $127.6m in our optimistic case, using a DCF valuation assuming certain levels of market penetration in relation to the indications (see below for the specific levels because they differ between our base and bull cases). Our valuation equates to 3.5c per share and 5.3c per share respectively assuming ~2.3bn shares on issue, taking into account our assumptions of capital raised up until FY27. Based on the current number of shares on issue derives 7.2c per share in our base case and 11.3c per share in our bull case.

We assumed that the company partners with a major healthcare company in a deal involving milestone payments upon the passage of Phase II and III clinical trials and the beginning of sales all adding up to ~$50m over the next five years. In return, this partner will receive a 50% share of revenues from commercial sales. The royalty revenues will cover the majority of R&D costs over the next 5 years (we assumed $35.4m in R&D expenses and a further $37.3m in employee expenses over that period). In addition, we have assumed the company raises $10m in FY24 in a further equity raising for general working capital and that it continues to receive modest R&D tax incentives. It goes without saying that if the company does not pursue a partnership, it will require substantial dilution to meet these capital requirements. Nevertheless, this scenario would mean 100% retention of revenues.

Our other main assumptions include:

- **WACC.** 10.5%, based on a 3.2% risk free rate of return (the rate of the 10-year government bond), an 8% equity premium and a 1.16 beta (based on the industry average for Healthcare Product Companies)[9].
- **Time horizon**. We used a 15-year time horizon in our DCF followed by a terminal value.
- **Launch year.** We model a soft commercial launch for HER2 breast cancer in FY27. This is followed by launch of prostate and ovarian cancer solutions by FY29, and brain cancer solutions by FY31.
- **Operating margins**. We assume that Imagion will become EBIT positive after four years, i.e., from 2027, and its EBIT margin will stabilise at 47-49% from 2030 onwards.
- **Tax.** We assumed a 30% tax rate.
- **Expenses.** As noted above, the majority of the company's costs will be R&D and employee expenses. We assumed modest cost inflation growth for professional fees, general expenses and share-based payment expenses. Depreciation is calculated as a modest % of the company's opening PPE book (on average 4%) while finance costs are calculated as a percentage of the company's lease liabilities (3.8%).

[9] https://pages.stern.nyu.edu/~adamodar/New_Home_Page/datafile/Betas.html

- **Base vs. optimistic (bull) case.** The two key differences between our base case and bull case assumptions pertain to:
  - **Market penetration –** In the base case, we have assumed Imagion's market penetration for HER2 breast cancer diagnosis to grow to 40% over the forecast horizon. Similarly, for prostate and ovarian cancer diagnostics, we have assumed market penetration to gradually reach 40%, and for brain cancer the corresponding value is 30%. Our bull case assumes 15% faster penetration. As a consequence, the comparable values in the bull case are 46% share for HER2 breast cancer, 46% share for prostate and ovarian cancer, and ~34% share for brain cancer.
  - **Product pricing –** We used US$1,500 (A$2,273) per test for the base case and US$2,000 (A$3,030) for the bull case and assumed 2.5% pricing increases annually. Using the above assumptions, we arrive at Imagion's valuation as shown in Figure 7. Figures 8 shows the different valuation using different WAACs.

Figure 7: DCF valuation for Imagion

Valuation (A$m)	Base case	Bull case
Present value of FCF	4.7	13.2
Present value of Terminal FCF	77.0	112.1
Enterprise Value	**81.8**	**125.3**
Net debt (cash)	(1.4)	(1.4)
Equity value	**83.1**	**126.7**
Share outstanding (FY 2022E)	2,303.7	2,303.7
Implied price (A$ cents)	**3.6**	**5.5**
Adjusted Current price (A$ cents)	1.6	1.7
Upside (%)	*125.5%*	*243.7%*

Source: Pitt Street Research

Figure 8: DCF value in A$ cents using various WACCs (base case)

Sensitivity						
WACC	**10.6%**					
Terminal Growth	**2.00%**					
Implied Price		*11.5%*	*12.5%*	*13.5%*	*14.5%*	*15.5%*
Change in Terminal Growth Rate	*1.25%*	5.2	4.2	3.4	2.9	2.5
	1.50%	5.3	4.3	3.5	2.9	2.5
	1.75%	5.4	4.3	3.5	3.1	2.5
	2.00%	5.4	4.3	**3.6**	3.0	2.5
	2.25%	5.4	4.5	3.7	3.3	2.6
	2.50%	5.4	4.5	3.8	3.5	2.6
	2.75%	5.5	4.6	3.8	3.5	2.6

Source: Pitt Street Research

Catalysts for a re-rating

We believe the following factors can contribute to the re-rating of Imagion in the direction of our valuation range:

- Successful results from phase 2 clinical trial in the US for patients with HER2-positive breast cancer.
- Meeting commercialisation milestones in relation to HER2-positive breast cancer in a timely manner.
- Encouraging results from studies and trials supporting the use of the MagSense technology for diagnosing prostate and ovarian cancers.
- Strategic collaboration or licensing agreement with any of the major medical technology players for Imagion's technology.
- Uptick in deal-related activity of larger medical technology companies which can improve the valuation of attractive mid-cap and small-cap players.

Potential deal-related upside for Imagion shareholders

We believe that acquisitions in the field of cancer diagnostics during the past five years are a strong indication of the attractiveness of this space. In 2018, Roche's acquisition of Foundation Medicine, which valued that company at US$5.3bn, was a landmark deal. Further, the 2018 acquisition of Sirtex Medical by the Chinese company CDH for A$1.9bn is another example. More recently, in 2022, LabCorp acquired Personal Genomics Diagnostics at a steep multiple of 14x sales.

Foundation Medicine was built on FoundationOne, a product that was the first fully informative cancer genomic profile that was 'pan cancer'. The FoundationOne test can detect mutations in more than 300 cancer-related genes and suggest implementable clinical action. Post-acquisition, Foundation Medicine obtained multiple companion diagnostic approvals for cancer and expanded its presence across 100 countries.

Sirtex Medical was a Sydney-based company founded in 1997 to commercialise SIR-Spheres, which are radioactive Yttrium 90 (Y-90) microspheres used in the treatment of liver cancer. Sirtex was listed on the ASX in August 2000 in order to commercialise SIR-Spheres. In September 2022, the company secured approval for using SIR-Spheres Y-90 resin microspheres for the treatment of hepatocellular carcinoma (HCC) in Brazil. In addition to Brazil, the product is approved for use in Argentina, Australia, Switzerland, Turkey and several other countries in Asia for HCC.

In H1 2022, **Personal Genome Diagnostics** (PGDx), a US-based cancer genomic start up, was acquired by LabCorp, for US$575m in an all-cash deal. The revenue of PGDx was expected to move up from US$22m in 2021 to US$40m in 2022. PGDx has a robust portfolio of enabling insights for patients with advanced cancer. PGDx's elio tissue and plasma complete test helps in non-invasive diagnosis of cancer. These are FDA-approved tumour profiling kits.

Key risks facing Imagion

We see four major risks for Imagion as a company and as a listed stock:

- **Funding risk**. Imagion currently has a funding commitment of ~A$18m that will help support the initial commercialisation activities. However, we estimate that the company will require further capital for commercialisation and R&D activities necessary for commercialisation. In case there is a delay in arranging further funding, it might impact the company's prospects and stock's valuation.
- **Execution risk**. There could be unexpected delays in the commercialisation process. Moreover, even after commercialisation, the company may not be able to penetrate the potential market at expected levels. Such setbacks will impact the cash flows and thus, valuation of the stock.
- **Clinical risk**. There is the risk that Imagion's clinical work with MagSense may not yield promising results for other oncology indications such as prostate, ovarian and brain.
- **Technology risk**. There is the risk that newer technologies with a superior cost profile in the personalised oncology space can emerge before Imagion has fully realised the commercial potential of MagSense.

Imagion has a strong management team

- **Robert Proulx**, the President and the CEO, has been associated with Imagion since February 2015, when the company was a subsidiary of Manhattan Scientific. Robert brings more than 25 years of experience in the life sciences and medical diagnostics sectors. He comes with significant experience and has worked in sales management and marketing roles.
- **Geoff Hollis,** the Chief Financial Officer and Company Secretary, has been associated with Imagion since December 2020. Prior to joining the company, Geoff worked as CFO and Company Secretary with Lifestyle Communities Limited, the fastest-growing, ASX-listed provider of residential accommodation.
- **Dr. Yalia Jayalakshmi**, Chief Development Offer, has been associated with Imagion since September 2021. She will be leading the global clinical development strategy and execution, while contributing to shape Imagion's strategic direction. She has ~25 years experience in the biopharmaceutical industry which includes R&D and product team leadership at J&J, PRD, Genentech, Onyx Pharma and Cygnus.
- **Dr. Marie Zhang**, VP Research and Preclinical Development, has been associated with Imagion since November 2018. Currently, she oversees the R&D team and directs the development of MagSense technology test reagents. She brings ~20 years of diverse experience to the company.
- **Dr. John Hazle, Chairman of Imagion's Scientific Advisory Board,** brings decades of thought leadership in the areas of image-guided therapy, pre-clinical imaging and early detection technologies.
- The company has an experienced board, comprising the following:
- **Michael Harsh**, Non-Executive Director, has been associated with Imagion since November 2016. Mike brings over 35 years of experience in the field of diagnostic imaging, having worked at GE Healthcare.
- **Jovanka Naumoska**, Non-Executive Director, is an Australian legal practitioner with significant experience in IP law, corporate law and corporate governance.
- **David Ludvigson**, Non-Executive Director, has been associated with Imagion since December 2016. He brings ~35 years of international experience in finance and operations in life sciences and technology companies, including IDEC Pharmaceuticals, Matrix Pharmaceutical, Nanogen and MIPS Computer Systems.
- **Mark Van Asten**, Non-Executive Director, brings ~30 years of experience in the medical diagnostics and life sciences industry. In his past roles, he spent a majority of his time in international business development, strategic planning and introduction of new technologies.
- **Dianne Angus,** Non-Executive Director, has worked as a senior executive within the biotechnology, agritech and healthcare sectors for over 20 years. Dianne has created many global industry partnerships to accelerate asset development, financing and provide reputational validation & endorsement. With eighteen years' experience in ASX and NASDAQ listed companies, Dianne has expertise in corporate governance, capital raising and stakeholder engagement within the listed capital market sector. Dianne holds a B.Sc. (Hons), M.(Biotechnology) and is a registered patent & trade mark attorney.

Companies to watch

The company has a unique technology proposition and there is a lack of pure-play, public-listed peers. Thus, in order to provide an idea of the broad competitive landscape for Imagion (Figure 10), we have screened companies using the following criteria:

1) Companies based in developed markets with market capitalisation lower than US$500m.
2) Public companies operating in health care equipment and biotechnology industries, focussing on cancer diagnostics.
3) Within cancer diagnostics too, we prioritised companies with imaging and non-invasive solutions.

Figure 10: Companies to watch

Public Company	Location	Ticker	Market cap (US$m)	Website
Cyclopharm Ltd.	Australia	ASX:CYC	93.3	www.cyclopharm.com
Predilife SA	France	ENXTPA:ALPRE	24.3	www.predilife.com
Ikonisys SA	France	ENXTPA:ALIKO	17.8	www.ikonisys.com
Izotropic Corp.	Canada	CNSX:IZO	15.6	www.izocorp.com
Spago Nanomedical AB	Sweden	OM:SPAGO	6.7	www.spagonanomedical.se
Imagin Medical Inc.	Canada	CNSX:IME	1.6	www.imaginmedical.com
Imagion Biosystems Ltd.	Australia	ASX:IBX	18.6	www.imagionbiosystems.com

Source: S&P Capital IQ, Pitt Street Research

Cyclopharm Ltd. (ASX:CYC) is engaged in manufacturing and selling medical equipment and radiopharmaceuticals in Asia Pacific, Europe and Canada. It operates through two segments – Technegas and Molecular Imaging segments. Through its Technegas segment, the company offers diagnostic equipment and consumables used by physicians in the detection of pulmonary embolism. The Molecular Imaging segment produces radiopharmaceuticals that are used by physicians in the detection of cancer, neurological disorders and cardiac diseases. The company was founded in 1986.

Predilife SA (ENXTPA:ALPRE) specialises in the development of predictive tests. The company offers prevention and breast check-up tests. Its products include MammoRisk, a test for predicting the development of breast cancer based on a patient's individual risk; and DenSeeMammo, a breast density measurement software. It also offers a medical device for the prediction of prostate cancer risk. The company was founded in 2004.

Ikonisys SA (ENXTPA:ALIKO) designs, manufactures and sells medical diagnostic equipment in the US and Europe. The company offers cell diagnostic products in the field of cancer diagnosis, genetic disorders and fertility testing. It offers Ikoniscope Robotic Microscope that provides automated slide handling, slide scanning, and real-time image capture and analysis; oncoFISH bladder that allows scanning and analysis of cells recovered from a voided urine sample; oncoFISH HER2, a microscopy application for the determination of the HER2 status of tissue sections from breast tissue biopsies; and oncoFISH anaplastic lymphoma kinase (ALK), a

microscopy application for the FISH based detection of rearrangements of the gene encoding anaplastic lymphoma kinase (ALK). The company was incorporated in 2021.

Izotropic Corp. (CNSX:IZO) is engaged in developing and manufacturing diagnostic products for breast cancer. It develops and commercialises breast CT Imaging system; and 3D CT breast imaging platform for the earlier detection and diagnosis of breast cancer. The company was incorporated in 2016.

Spago Nanomedical AB (OM:SPAGO) is a nanomedicine company engaged in developing products for cancer diagnostics and treatment. It is involved in the development of SN132D, a gadolinium-free MRI contrast agent for the treatment of breast and pancreas cancer under the SpagoPix project; and SN201, a radionuclide therapy for treatment of advanced and metastatic cancer under the Tumorad project. The company was incorporated in 1999.

Imagin Medical Inc. (CNSX:IME) operates as a urologic oncology company. Its products include i/Blue Imaging System, which detects bladder cancer with advanced optics and light sensors; and enCage Coil, a focal therapy precision ablation device used in the treatment of prostate cancer. It is also developing technologies to treat urologic cancers (including bladder and prostate cancer) through minimally invasive surgery. The company was founded in 1986.

Appendix I – Glossary

Antibodies – Immune system proteins that can bind to an antigen and help neutralise the potentially harmful effects of the cells carrying the antigen. Antibodies are often used in diagnostics.

Antigens – A foreign substance capable of inducing an immune response in the body, especially the production of antibodies.

Biopsy – Removal of a sample of tissue from the body for diagnostic purposes.

Biomarker – A naturally occurring molecule/gene/characteristic that can be used to detect or diagnose any physiological condition.

GMP – Short for Good Manufacturing Practice; the set of standards laid down by regulators such as the FDA for the production of clinical-grade pharmaceuticals. cGMP refers to 'current' Good Manufacturing Practice, since GMP standards tend to change over time.

HER2 – The protein targeted by the cancer antibody drug Herceptin that is overexpressed on breast cancer cells.

Ligand – An ion or molecule that binds to central metal atom to form a coordination complex.

Liquid biopsy – A test done on a sample of blood to look for cancer cells from a tumour that are circulating in the blood or for pieces of DNA from tumour cells that are in the blood.

Lymph nodes – Points in the lymphatic system rich in immune system cells designed to filter harmful substances.

Magnetometer – An instrument that measures the direction and/or strength of a magnetic field.

MagSense – Imagion's diagnostic imaging technology, which involves nanoparticles, labelled with cell-specific antibodies, which are re-magnetised and their location detected using SQUID.

Magnetomotive ultrasound imaging – A technique under development that indirectly visualises nanoparticles.

Magnetic relaxometry (MRX) – A technique utilising super-paramagnetic nanoparticles to detect various diseases using antibodies.

Nanoparticle – Any microscopic particle less than about 100 nanometres in diameter.

Radiotracer – A chemical compound in which one or more atoms have been replaced by radionuclide; these compounds are used to explore the mechanisms of a chemical reaction by tracing the path that radioisotope follows from reactants to products.

SQUID – Short for Superconducting Quantum Interference Device, a highly sensitive magnetometer made up of Josephson junctions.

Superparamagnetic – A form of magnetism that appears in small ferromagnetic or ferromagnetic nanoparticles.

Superparamagnetic relaxometry – A technology that uses SQUID sensors and superparamagnetic nanoparticles to detect cancer and other diseases.

Appendix II – Capital structure

Class	In million	% of fully diluted
Quoted securities		
Ordinary shares on issue	1,121	79.4%
Unquoted		
Options and performance rights	290.0	20.6%
Fully diluted shares	**1,411.0**	

Source: Company

Appendix III – IP position

Imagion's intellectual property derives from the following applications:

US 2020, 0187822, *Detection, measurement, and imaging of cells using cellular internalization of nanoparticles,* priority date 15 December 2018, invented by Edward R. Flynn and Erika Vreeland.

- The patent discloses a method for detecting, measuring and locating cancer cells in a patient. It involves the administration of targeted super paramagnetic nanoparticles to the patient for internalisation by cells, which are then detected by applying magnetic field and analysing residual field using superconducting quantum interference device (SQUID) magnetic sensors. The method uses iron-oxide-based magnetic nanoparticles comprising targeting agents, such as specific antibodies, proteins and macromolecules. The magnetic systems allow early detection of cancers such as prostate and breast cancer by detecting sub-nanogram amounts of nanoparticles.
- Application for the patent was filed only in the US, which also was abandoned in 2022 due to a failure to respond to an office action (the patent might be revived using appropriate corrective actions).

US 2020, 0188537, *Methods and apparatuses for the detection of disease such as cancer,* priority date 14 December 2018, invented by Edward R. Flynn.

- The patent pertains to a method for detecting, measuring and locating cancer cells to enable the targeted delivery of hypothermia therapy – i.e., exposure to high temperatures to damage/kill cancer cells – and

monitoring of its effects. The method involves the administration of targeted super paramagnetic nanoparticles – iron-oxide-based magnetic nanoparticles comprising targeting agents, such as specific antibodies, proteins and macromolecules – to the patient for internalisation by cells. The nanoparticles are then detected by applying magnetic field and analysing residual field using superconducting quantum interference device (SQUID) magnetic sensors.

– Application for the patent was filed only in the US. The patent is yet to be granted.

WO 2022, 060924, *Methods and apparatuses for the synthesis of drug-loaded magnetic micelle aggregates,* priority date 16 September 2020, invented by Konstantin Sokolov, Marie Zhang, Chang Soo Kim, Dmitry Nevozhay, Rebeca ABURTO, Ashok Pehere, Lang PANG, John Hazle, Robert Clinton BAST.

– The patent discloses a one-step method to produce magnetoliposomes that involves the infusion of a mixture containing hydrophobic lipids and uniform oleic-acid-coated magnetic nanoparticles (with core diameter ~25 nm) in chloroform with a hydrophilic drug-containing aqueous phase, followed by ultrasonication. It uses optimised lipid-to-iron oxide nanoparticle ratio, flow speed and sonication power to generate reproducible, stable and uniform liposomes comprising encapsulated iron oxide nanoparticles and a soluble anti-cancer drug, doxorubicin. The magnetoliposomes further feature targeting antibodies to ensure high specificity for treating cancer such as breast cancer.

– Only a WIPO application has been filed till date (WIPO applications are filed under the Patent Cooperation Treaty, which harmonises the patent application process among member nations).

Appendix IV – Papers relevant to Imagion

Zhi Wei et al. (2017), *The Relaxation Wall: Experimental Limits to Improving MPI Spatial Resolution by Increasing Nanoparticle Core size.* Biomed Phys Eng Express, Volume 3, Issue 3, Page 035003.

The paper pertains to a study conducted to understand the effect of increasing the magnetic core size of superparamagnetic nanoparticle tracers on the spatial resolution of magnetic particle imaging (MPI). Ideally the spatial resolution increases with an increase in nanoparticle core size – according to the steady-state Langevin physics model – however, the study showed that it only improved till a certain core size, i.e., 25 nm, which was found to be optimal for conducting MPI. This was a result of the magnetic blurring caused by magnetic relaxation – the process of a material's magnetization returning to its equilibrium state due to an external magnetic force or any disturbance – caused by the large size of nanoparticles.

Leibl et. al. (2015), *Magnetorelaxometry procedures for quantitative imaging and characterisation of magnetic nanoparticles in biomedical applications.* Biomed Tech (Berl). 2015 Oct;60(5):427-43.

In this article, researchers review magnetorelaxometry (MRX) based procedures that enable both the characterisation and the quantitative imaging of MNPs in a biomedical environment.

De Haro et. al. (2015), *Magnetic relaxometry as applied to sensitive cancer detection and localisation.* Biomed Tech (Berl). 2015 Oct;60(5):445-55.

This article describes superparamagnetic relaxometry (SPMR), a technology that uses highly sensitive magnetic sensors and superparamagnetic nanoparticles for cancer detection. Using SPMR, researchers sensitively and specifically detected nanoparticles conjugated to biomarkers for various types of cancers. In addition, the technology offered high contrast in vivo, as there was no superparamagnetic background, and bones and tissue were transparent to magnetic fields.

Butler et. al. (2013), *Development of antibody-tagged nanoparticles for detection of transplant rejection using biomagnetic sensors.* Cell Transplant. 2013;22(10):1943-54. Epub 2012 Oct 12.

This study illustrated the development of antibody-tagged nanoparticles for the detection of transplant rejection using biomagnetic sensors.

Johnson et. al. (2012), *Magnetic Relaxometry with an Atomic Magnetometer and SQUID Sensors on Targeted Cancer Cells.* J Magn Mater. 2012 Aug 1;324(17):2613-2619.

This study involved magnetic relaxometry using both atomic magnetometers (AM) and SQUID sensors to detect cancer cells that are coated with superparamagnetic nanoparticles through antibody targeting.

Adolphi et. al. (2012), *Imaging of Her2-targeted magnetic nanoparticles for breast cancer detection: comparison of SQUID-detected magnetic relaxometry and MRI.* Contrast Media Mol Imaging. 2012 May-Jun;7(3):308-19.

This study analysed the detection of single-core iron-oxide nanoparticles by SQUID-detected magnetic relaxometry, as well as by standard 4.7 T MRI. The nanoparticles were conjugated to a HER2 monoclonal antibody and targeted to HER2-expressing MCF7/HER2-18. The binding of nanoparticles to the cells was assessed by magnetic relaxometry and iron assay. The results demonstrated the potential of SQUID-detected magnetic relaxometry imaging for the specific detection of breast cancer.

Hathaway et. al. (2011), *Detection of breast cancer cells using targeted magnetic nanoparticles and ultra-sensitive magnetic field sensors*. Breast Cancer Res. 2011 Nov 3;13(5):R108.

This research publication highlights the promising nature of antibody-conjugated magnetic nanoparticles to be used in in vivo breast tumour cell detection. Additionally, it analyses SQUID-detected magnetic relaxometry as a viable, rapid and highly sensitive method for in vitro nanoparticle development and eventually in vivo tumour detection.

Appendix V – 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, and numerous other 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 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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