PITT STREET RESEARCH

Imagion Biosystems

Breakthrough device

Share Price: A$0.039

Valuation range: A$0.12-0.26

ASX:IBX

Sector: Health Care Equipment & Services

26 September 2019

An innovative medical device company

Imagion Biosystems (ASX: IBX) is an Australian medical device company whose MagSense diagnostic imaging technology, currently in early stage development, can potentially improve on PET and MRI imaging modalities. Imagion is currently in preclinical development with the first human pilot studies of the technology intended for 2020. The FDA granted MagSense a Breakthrough Device designation in July 2019.

Imagion goes to the clinic next year

Imagion intends to undertake a first-in-human study of the MagSense technology initially in HER2-positive breast cancer to be followed later in prostate cancer and ovarian cancer. With HER2-positive breast cancer the goal will be to establish a non-invasive method of detection of cancer in the lymph nodes compared to conventional biopsy of the sentinel lymph nodes.

Another beneficiary of the personalised medicine trend

Pitt Street Research believes that the mid-2018 acquisition by Roche of Foundation Medicine, which valued that company at US$5.3bn, was a landmark transaction from the perspective of Imagion shareholders. The 2018 acquisition of Sirtex Medical by the Chinese company CDH for A$1.9bn, and the current market capitalisation on ASX of Telix Pharmaceuticals are also possible comparisons since in each case these companies combined a radiotracer with treatment. Obviously, Imagion is going after detection first, but the company has the same long-term promise of being able to be used for treatment as Sirtex and Telix.

Potential first sales from 2023

Imagion intends to sell MagSense on a 'printer and ink' model where a low sales price for the SQUID equipment (US$0.5m at a 50% gross margin) is matched with a relatively higher selling price for the nanoparticles (US$1,500 per test for an 80% gross margin). Pitt Street Research argues that, potentially, Imagion can look to make its commercial launch in 2022 or 2023.

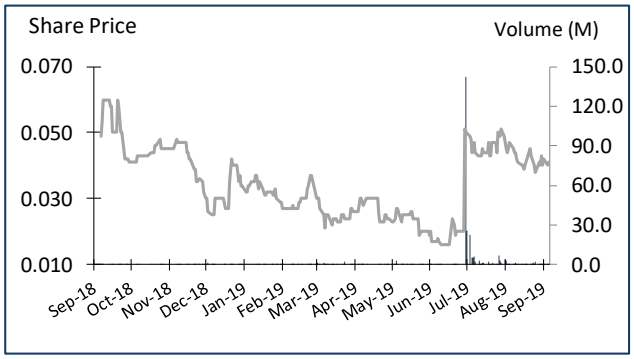
Imagion is undervalued on our numbers

We value Imagion at 12 cents base case and 26 cents optimistic case on a risk weighted DCF basis. We see Imagion being re-rated towards our valuation range on the back of improved sentiment towards MagSense as a Breakthrough Device, as the company takes the device into the clinic.

Market Cap. (A$ m)	12.6
# shares outstanding (m)	323.7
# share fully diluted	377.5
Market Cap Ful. Dil. (A$ m)	14.7
Free Float	100%
12 months high/low (A$)	0.06 / 0.016
Average daily volume (x1,000)	121
Website	imagionbiosystems.com

Source: Company, Pitt Street Research

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



Source: Thomson, Pitt Street Research

Valuation metrics	
Fair valuation (A$)	$0.12-$0.26
WACC	13.6%
Assumed terminal growth rate	3-5%

Source: Pitt Street Research

Subscribe to our research HERE

Analyst: Stuart Roberts

Tel: +61 (0)4 4724 7909

stuart.roberts@pittstreetresearch.com

Table of Contents

Introducing Imagion Biosystems 3

Ten reasons to look at Imagion Biosystems 5

MagSense bridging gap between traditional imaging and newer screening technologies 6

MagSense conceptualised in late 1990s; Imagion fast-tracked its development in recent years 6

Technology involves delivery of payloads attached to nanoparticles to locate/quantify tumour cells 7

Specialised and distinct nanoparticles are prepared for each tumour cell-type 8

Imagion's nanoparticles can be used in various ways 9

MagSense is significantly superior to other imaging modalities, such as MRI or CT scan 9

HER2 breast cancer indication initially targeted by Imagion for commercial market access 10

Breakthrough Device designation, a critical milestone in de-risking Imagion's clinical programme 11

Imagion's technology has potential to tap major markets of cancer diagnostics 11

Breast cancer – the leading indication for commercialisation 12

Prostate cancer – a long-term market opportunity for Imagion 13

Ovarian cancer is another indication targeted by Imagion 13

Valuing Imagion Biosystem 14

Re-rating Imagion Biosystems 15

Imagion Biosystems has a strong management team 16

Appendix I – Glossary 17

Appendix II – Capital structure 18

Appendix III – IP position 18

Appendix IV – Papers relevant to Imagion Biosystems 20

Appendix V – Major shareholders 22

Appendix VI – Companies to watch 23

Appendix VI – Risks related to Imagion 24

Appendix VII – Analyst qualifications 25

General advice warning, Disclaimer & Disclosures 26

Introducing Imagion Biosystems

A diagnostic imaging technology, which is set to make its clinical entry in 2020

Imagion Biosystems (ASX:IBX) (Imagion) is a diagnostic imaging technology developer. Imagion Biosystems is an Australian medical device company whose MagSense diagnostic imaging technology, currently in early stage development, can potentially improve on PET and MRI imaging modalities. Imagion is currently in preclinical development with the first human pilot studies of the technology intended for 2020. The FDA granted MagSense a Breakthrough Device designation in July 2019.

Imagion's MagSense technology is orders of magnitude better than MRI or CT. The MagSense technology involves magnetizable iron oxide nanoparticles conjugated to target-specific monoclonal antibodies where the nanoparticles can be detected using highly sensitive 'SQUID' magnetometers. MagSense is potentially better than PET or MRI because it would not involve radioactivity like PET and use less powerful magnetic fields than MRI. The initial indications for MagSense are in detection of cancer. MagSense works as a superior imaging tool because the magnetic property of the bio-safe nanoparticles allows the SQUID device to detect the nanoparticles only when the antibody has bound to its target. The monoclonal antibody binding the nanoparticles to the target tumour tissue cause the magnetic nanoparticle to 'relax', that is, lose their induced magnetism, at a slower rate than unattached particles. Imagion believes that the MagSense technology is 1000-times more sensitive than CT scans[1], with tumours smaller than one millimetre potentially able to be detected. The MagSense instrument is expected to cost considerably less than conventional MRI or CT machines. The combination of high sensitivity and specificity at low cost and high speed suggests a potential to detect more cancers when they are still at an early stage.

MagSense is at an early stage of development but the technology has been granted Breakthrough Device designation. Imagion inherited a technology that was first developed in the late 1990s but had yet to proceed into the commercialisation phase[2]. Since it went public on ASX in mid-2017, Imagion has 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 to GMP standards, which will be needed for clinical testing[3], and in late 2018 the company started working with Planet Innovation, a healthtech innovation and commercialisation company based in Melbourne [4], on instrument development. Imagion commenced pre-clinical safety and toxicology studies for its lead indication in February 2019 ahead of the entry of MagSense into the clinic, expected in 2020. The FDA granted MagSense a Breakthrough Device designation in July 2019.

MagSense will enter the clinic next year. Imagion intends to undertake a first-in-human study of the MagSense technology initially in HER2-positive breast cancer (targeting HER2 expression), to be followed later in prostate cancer (e.g., targeting PSA) and ovarian cancer (e.g., targeting CA125). The initial clinical programme will be in HER2-positive breast cancer, where the goal is to establish a non-invasive method of detection of cancer in the lymph nodes compared to conventional biopsy of the sentinel lymph nodes. The Breakthrough Device designation from the FDA is expected to speed the regulatory process of MagSense for the breast cancer indication.

[1] That is, MagSense has a detection threshold of less than 1 million cells.
[2] MagSense was originally developed by the nuclear physicist Dr Edward Flynn, who until the late 1990s was a researcher at Los Alamos National Laboratory. In the late 1990s Flynn founded a company called Senior Scientific to develop the MagSense technology. Senior Scientific was acquired in 2011 by a New York-based Manhattan Scientifics (New York, NY, OTCQB: MHTX, mhtx.com). Imagion Biosystems was formed in 2016 to acquire the MagSense project from Manhattan Scientifics and moved it from Albuquerque, NM to San Diego, CA.
[3] See the Imagion market release dated 10 September 2018 and headlined '*Imagion Biosystems hits nanoparticle formulation milestone*'.
[4] See planetinnovation.com.

Proposed business plan post first approval

Imagion intends to sell MagSense on a 'printer and ink' model where a low sales price for the SQUID equipment (US$0.5m at a 50% gross margin) is matched with a relatively higher selling price for the nanoparticles (US$1,500 per test for an 80% gross margin). Pitt Street Research argues that, potentially, Imagion can look to make its first filing for regulatory approval in 2023.

Potential upside for Imagion shareholders

Recent acquisitions in the field of cancer diagnostics space is a clear indicator of lucrative opportunity from Imagion

Pitt Street Research believes that the mid-2018 acquisition by Roche of Foundation Medicine, which valued that company at US$5.3bn, was a landmark transaction from the perspective of Imagion shareholders. The 2018 acquisition of Sirtex Medical by the Chinese company CDH for A$1.9bn, and the current market capitalisation on ASX of Telix Pharmaceuticals are also possible comparisons since in each case these companies combined a radiotracer with treatment. Obviously, Imagion is going after detection first, but the company has the same long-term promise of being able to be used for treatment as Sirtex and Telix.

- Foundation Medicine was built on FoundationOne, a product, which at its 2012 launch 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. The size of the 2018 deal represents Roche's optimism on the future of personalised cancer medicine, however we argue that it is also relevant to Imagion because it indicates the upside from new-generation cancer diagnostics where that diagnostic is a breakthrough compared to previous modalities.
- Sirtex Medical was a Sydney-based company founded in 1997 to commercialise SIR-Spheres, which are radioactive Yttrium 90 microspheres used in the treatment of liver cancer. Sirtex was listed on the ASX in August 2000 in order to commercialise SIR-Spheres. By FY16 Sirtex had grown its annual sales revenue to A$232m and NPAT to A$54m.
- Telix Pharmaceuticals[5] is developing a number of radiotracer products conjugated to monoclonal antibodies. The lead programme is a renal cancer diagnostic in phase 3 and earlier programmes are being developing in metastatic prostate cancer and glioblastoma. As at 25 September 2019, Telix had a market capitalisation on ASX of ~A$396m.

If Imagion Biosystems is so good, how come it is currently capitalised on ASX at only A$12.6/US$8.6m?

Imagion went public on the ASX in June 2017 after raising A$12m at 20 cents per share. The share price has never closed above 20 cents since then and in late 2018, the company was raising new capital at 4 cents per share. Even the Breakthrough Device designation news of July 2019 has failed to take Imagion above US$20m. We think the delays in completing the MagSense device has been the main problem with investor sentiment. We see Imagion re-rating as the device moves into its clinical studies in Her2.

[5] Melbourne, Australia, ASX: TLX, telixpharma.com.

Ten reasons to look at Imagion Biosystems

1) **MagSense is an important improvement on the standard of care,** allowing more sensitive, specific and safe detection of cancer at a much earlier stage of development than competing modalities such as CT and MRI scans.
2) **MagSense has achieved Breakthrough Device designation.** The July 2019 Breakthrough Device designation by the FDA for MagSense in Her2-positive breast cancer was an important development for Imagion. It not only allows expedited dialogue with the Agency but also recognises that MagSense is more than 'just another device'.
3) **The business opportunity for Imagion with MagSense is large**, given that cancer diagnostic tools represent a US$100bn market globally and the largest share of that market represents diagnostic imaging.
4) **The market opportunity for Her2-positive breast cancer is particularly significant**, since the use of MagSense in this cancer can eliminate lymphadenectomy in possibly 50% of patients, as well as remove uncertainties related to mammograms. There are ~50,000 new cases of Her2-postive breast cancer in the US annually.
5) **MagSense goes to the clinic soon**, with the first-in-human study of the product expected to commence in early 2020, potentially allowing the first pivotal study to commence by late 2021.
6) **MagSense has received some important validation from investigators**. Imagion has had a five-year collaboration at the MD Anderson Cancer Centre in Houston, Tx. We regard the decision by MD Anderson Cancer Centre to take an equity stake in Imagion in May 2018, in lieu of payment for part of the sponsored research programme, as encouraging validation on the part of key opinion leaders.
7) **The business plan for Imagion is compelling,** with Imagion proposing to sell MagSense on a 'printer and ink' model where a low sales price for the equipment is matched with a relatively higher selling price for the nanoparticles. This approach has been the basis of success for many medical equipment companies and should allow rapid sales growth so long as the clinical data validates the MagSense approach.
8) **Imagion has a strong leadership team.** Imagion's Executive Chairman is **Bob Proulx**, whose background in medical devices includes a period as President of Silicon Biosystems, developer of a liquid biopsy diagnostic system. The other directors of Imagion are **Mike Harsh** (a long-time head of diagnostic imaging engineering at GE), **Bronwyn Le Grice** (an Australian medical device entrepreneur), **David Ludvigson** (a US Life Sciences entrepreneur), **Jovanka Naumoska** (an Australian corporate lawyer) and **Mark Van Asten** (an Australian diagnostic entrepreneur). Imagion's CFO, **Brian Conn**, has a long track record of working on the financial side of small biotech and medical device companies. VP of R&D **Dr. Marie Zhang** brings chemistry smarts gained at various biotech companies over the last 25 years.
9) **Imagion has achieved a great deal with only limited funding**. Imagion raised A$12m at IPO and another A$4.3m in a 2018 rights issue. A key strength of Imagion is the fact that it is a US-based R&D organization with a management team and board familiar with the US Life Sciences scene, but it has the tax credit advantages of having an Australian parent company. The company received A$2m in R&D tax incentive payments in July 2019.

10) **Imagion is undervalued on our numbers**. We value Imagion at 12 cents base case and 26 cents optimistic case on a risk-weighted DCF basis. We see Imagion being re-rated towards out valuation range on the back of improved sentiment towards MagSense as a Breakthrough Device, as the company takes the device into the clinic.

MagSense bridging gap between traditional imaging and newer screening technologies

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 the target cells. The technology is being developed to provide a high-level overview of cancer cells, i.e., location of tumour, size of tumour and details such as molecular specificity. Imagion plans to expand the applications of the technology other areas such as delivering therapeutics to targeted cells or diagnosing diseases other than cancer. In February 2019 the company received an important US patent (No. 10,194,825) to include both detection and treatment.

Currently, the MagSense technology is being investigated for the detection and diagnosis of solid cancerous cells, such as those present in breasts, prostate or lungs. We believe that the technology can be further expanded to other indications once the proof-of-concept is established.

MagSense conceptualised in late 1990s; Imagion fast-tracked its development in recent years

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, 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.

MagSense technology is set to make its clinical entry in 2020; it received Breakthrough Device designation from USFDA in July 2019

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 will be needed for clinical testing, and in November 2018, it signed a partnership agreement with Planet Innovation, a healthtech innovation and commercialisation company based in Melbourne, to engineer instrument technology for clinical use and to obtain the required regulatory and commercial clearances. Imagion commenced pre-clinical safety and toxicology studies for its lead indication in February 2019 ahead of MagSense's clinical entry, expected in 2020. The FDA granted MagSense the Breakthrough Device designation in July 2019.

The company's initial commercialisation plan is focussed on the development of a floor-standing measuring instrument with one or more magnetising coils and a small number of SQUID-magnetometer sensors (Figure 1).

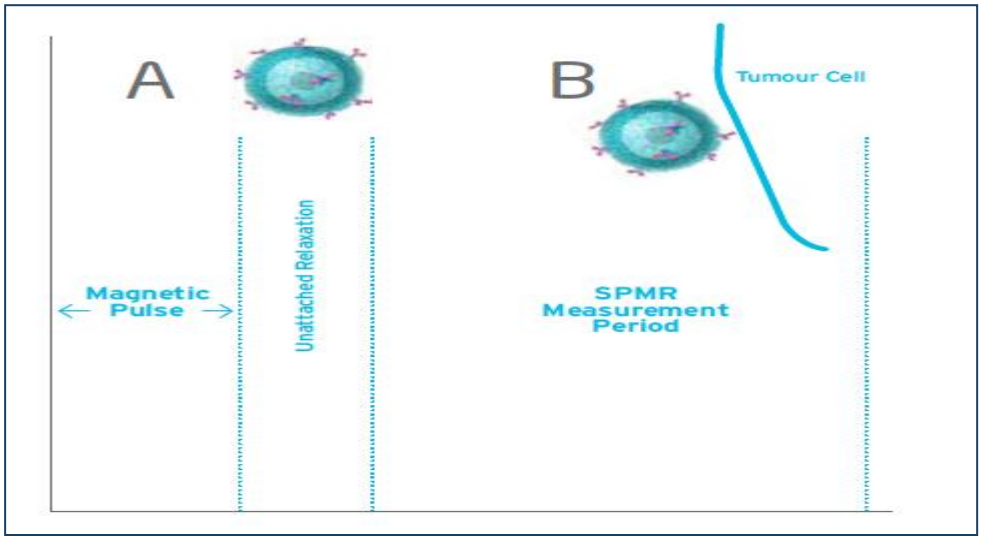
Figure 1: MagSense instrument

Source: Company

Technology involves delivery of payloads attached to nanoparticles to locate/quantify tumour cells

The MagSense technology uses the unique properties of specialised nanoparticles to locate and quantify diseased areas, such as cancer, present in the human body based on their distinct cell features. These nanoparticles are conjugated with antibodies or small molecules to enable them to bind with specific antigens present on the surface of the target cells. Upon binding, the nanoparticles exhibit a unique magnetic signature, which is not exhibited by any other structure in the human body (including unbound nanoparticles). As can be seen in the Figure 2, nanoparticles (particle B) that are attached to tumour cells relax from the magnetised state at a slower rate than particles that are free of attachment (particle A).

Figure 2: Magnetising particles and measuring relaxation time in few seconds



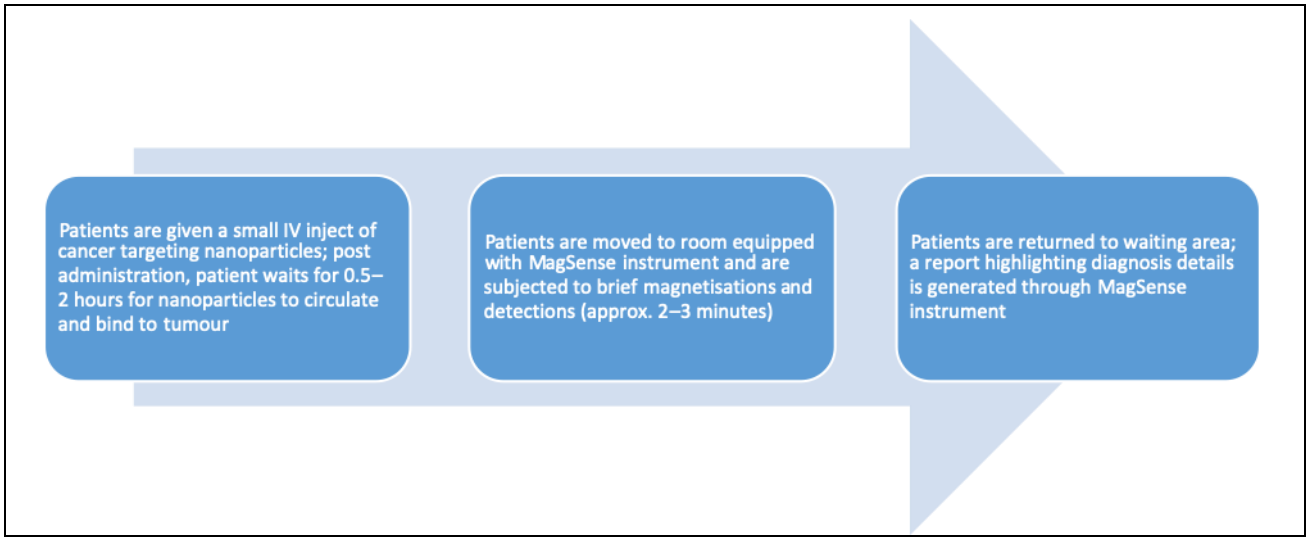
Source: Company

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

The detection of a magnetic signature allows the identification and quantification of targeted cells (*e.g.* cancer cells), without the interference from any other substance/tissue in the human body. The physics and principles of magnetic relaxation of bounded nanoparticles are well characterised by and described within the research community as superparamagnetic relaxometry (SRPM), which is being employed by the company for detecting different types of tumours, including prostate, ovarian or breast tumour cells. This is the basis of Imagion's core patent, which has been issued in seven countries and is pending in the EU.

Figure 3 highlights the expected clinical procedure through the use of the MagSense technology. A typical MagSense procedure will involve administration of a small intravenous injection (or injection via another route of administration) of cancer-specific targeting nanoparticles to patients. Post 0.5–2 hours of administration, patients will be moved to a room equipped with a MagSense instrument, and exposed to a series of magnetisations and detections resulting in a detailed report.

Figure 3: Expected MagSense clinical procedure



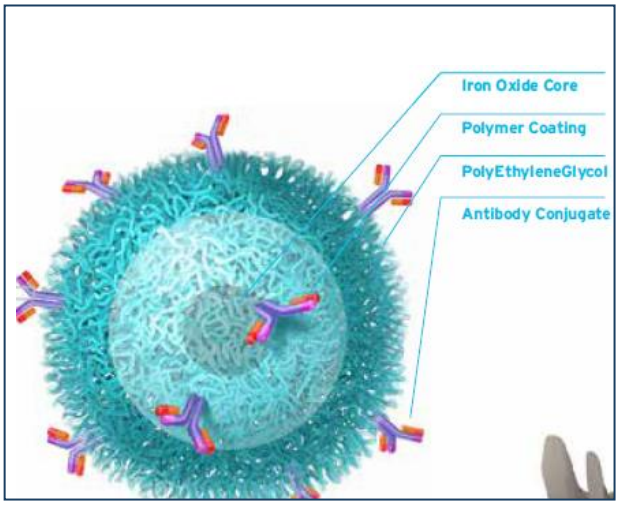
Source: Company

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

Superparamagnetic 25 nm magnetite (Fe_3O_4) nanoparticles are fabricated to perform MagSense-based detection/diagnosis

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 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 nanoparticles, the formulation will be packaged and supplied to customers by Imagion or a commercialisation partner 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 early animal studies, Imagion has found that nanoparticle volumes administered to patients have a wide tolerance.

Imagion contracted a Dutch drug manufacturer, ChemoConnections, in October 2017, to make the company's first clinical-grade nanoparticles for the detection of HER2 breast cancer.

Imagion's nanoparticles can be used in various ways

The nanoparticles can also be applied to other applications, such as MRI or magnetomotive ultrasound imaging

Imagion's nanoparticles have multiple potential uses:

- They could enhance T2 relaxation and the observed T2* signal in MRI, allowing them to enhance lymph node, bone marrow and perfusion imaging. The changes in nanoparticles-uptake and -clearance rates from previous or expected values indicate an alteration in cellular function – enabling better diagnosis.
- They could be used in magnetomotive ultrasound imaging (MMUS), wherein the pulse magnetic field is used for inducing motion of tissue-associated aggregations of magnetic nanoparticles.
- They could be antibody-conjugated to cells of interest through immune recognition, allowing cells to be reversibly captured in a magnetic field for separation from unwanted cell types.

MagSense is significantly superior to other imaging modalities, such as MRI or CT scan

The MagSense technology uses highly sensitive magnetic field sensors to detect the remnant magnetic relaxation of the injected nanoparticles. The MagSense systems are expected to be inexpensive as the underlying

technology utilises a small number of sensors for localised disease detection as well as low magnetic field, unlike other expensive imaging technologies, which require strong magnetic fields and full-body scanning.

Moreover, the company expects the technology will not require a shielded operating environment for the processing of images through the systems. They can be installed in a standard hospital facility without additional expenditure on special and expensive facility engineering. Apart from being cost effective, MagSense technology offers a number of benefits over currently available conventional imaging technologies such as ultrasound or X-rays. These include the following:

- **Limited adverse effects:** Surrounded tissues do not adversely impact the results generated by the MagSense technology, as small magnetic field emanating from nanoparticles freely traverses the surrounding tissues.
- **Higher sensitivity:** The instrument uses highly sensitive magnetic sensors, which allows the use of low magnetic fields (<<MRI) – believed to be safe for patients. Imagion's system is 1,000 times more sensitive than other imaging modalities such as CT scan.
- **High-level cell differentiation:** MagSense technology comes with an ability to differentiate benign tumours from malignant ones as the antibody-conjugated nanoparticles selectively bind to targeted tumour cells – differentiation is not possible by the use of conventional imaging technologies.
- **High specificity:** The use of antibody-targeted nanoparticles ensures the specificity of tumour detection and minimises the risk of false-positive results. Further, the technology comes with an ability to detect tumours as small as one mm using the power of magnetisation.
- **Multiple purposes:** A single MagSense instrument can be used for the diagnoses of multiple cancers and this improves the return on investment for the hospitals.
- **More than a just a detection procedure:** Imagion's technology not only identifies the 'region of interest', but also locates and quantifies it. This feature is not exhibited by currently available imaging modalities such as MRI and CT scan.

MagSense will perform localised detection of tumours; it could be further developed to increase the area of detection

HER2 breast cancer indication initially targeted by Imagion for commercial market access

As part of its market entry strategy, Imagion's initial aim is to commercialise its proprietary technology for monitoring the progression and staging of HER2-positive breast cancer[6], which is one of the most prominent types of cancer. Each year, almost 15–20% of the 2 million breast cancer patients globally are generally affected by HER2-positive breast cancer. This translates into 240,000–320,000 patients with HER2-positive breast cancer every year. This patient population represents a significant addressable market for diagnostics companies, such as Imagion. As of now, the MagSense technology is anticipated to make its entry into the clinic in 2020. We believe that the company's first marketing approvals will markedly lift the value of Imagion as a company as well as a listed stock. In terms of the total addressable opportunity, we estimate that the initial market for the technology in HER2 breast cancer will be worth ~US$0.6bn, considering that 20% of the total 2 million breast cancer patients can take Imagion's test for monitoring/staging HER2-positive breast cancer at a price of US$1,500 per test.

[6] Progression refers to expansion in the size of individual tumours. Staging refers to the level of spread of the cancer through the body.

Currently, a number of procedures are available for the diagnosis and staging of breast cancer. These typically include use of mammography, MRI or ultrasound, and lymph node biopsy – the latter being the definitive means of diagnosis and staging of breast cancer. However, these procedures are neither economical nor safe (invasive in nature) for patients, as they require the collection of target tissue to carry out diagnostic operations. There is a significant unmet need of 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 diagnostics modality for the monitoring of breast cancer disease progression.

Breakthrough Device designation, a critical milestone in de-risking Imagion's clinical programme

HER2-positive indication is the initial indication for which Imagion received Breakthrough Device designation

Recently, Imagion received the Breakthrough Device designation from the Centre for Devices and Radiological Health (CDRH) of the United States Food and Drug Administration (USFDA). Granting of the Breakthrough Device designation to Imagion's MagSense system and its test for HER2-positive breast cancer staging represents a significant achievement for Imagion, as this designation is granted only to those devices that are anticipated to provide an effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions. The designation granted to MagSense system and associated test for HER2 breast cancer is a clear indicator of transformative opportunity for healthcare. In addition, it validates MagSense's ability to improve the standard of care for staging HER2-positive breast cancer. Imagion's device is aimed at eliminating unnecessary surgeries and concomitant morbidities that result from the current standard-of-care biopsy procedures. The device is expected to emerge as a non-invasive and non-radioactive procedure, which will be used for detecting the presence and progression of HER2-positive breast cancer.

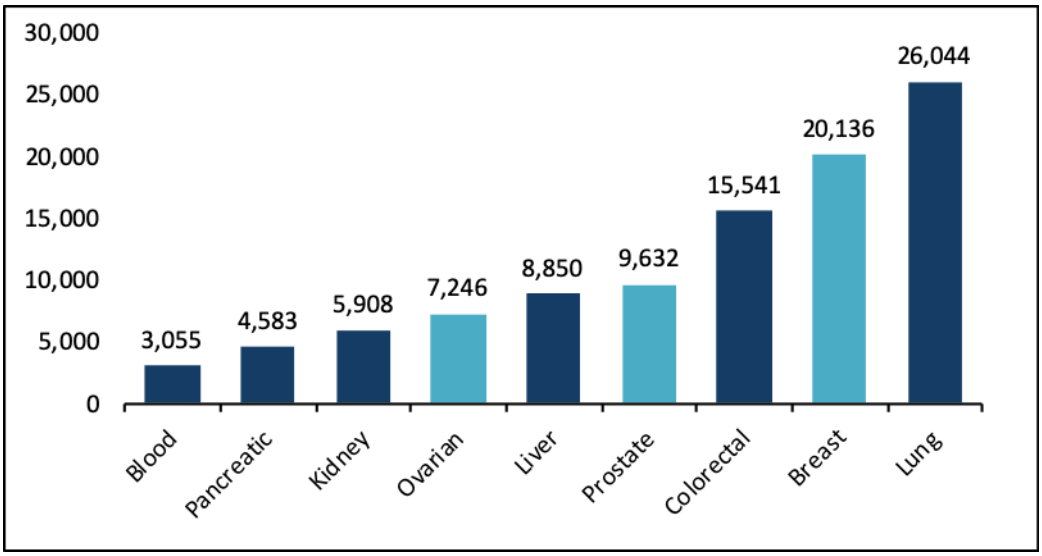
Unlike current biopsy procedures, Imagion's MagSense system would not require the removal of tissue from the patient; rather, it will non-invasively detect/monitor the progression of HER2-positive breast cancer by delivering targeted nanoparticles to tumour cells.

Apart from fast-tracking the approval process for MagSense system, the grant of Breakthrough Device designation is expected to improve communication between the device manufacturer – Imagion – and the agency (USFDA) during device development and the review process of MagSense system and associated tests. Considering the benefits involved, we believe that the grant of this designation by the USFDA represents an important advantage for Imagion in its commercialisation plans.

Imagion's technology has potential to tap major markets of cancer diagnostics

The development of MagSense technology will allow Imagion to make an entry into the lucrative market of cancer diagnostics, which is expected to reach US$100bn by 2020, according to Transparency Market Research. Imagion aims to commercialise its technology for breast, prostate and ovarian cancers. Estimates suggest that by 2020, global annual spending on the diagnosis of breast, prostate and ovarian cancers is anticipated to exceed US$20bn, US$9bn and US$7bn, respectively (Figure 5).

Figure 5: US$100bn global cancer diagnostics market[7]



Source: Transparency Market Research

MagSense technology will address most of the bottlenecks associated with currently available imaging modalities

The increase in diagnostics spending is a clear indicator of the upcoming opportunity for Imagion in the field of cancer diagnostics. Within cancer diagnostics spending, diagnostic imaging captures the major share of global spending, whereas biopsy- and biomarker-based diagnostics account for a small proportion of the total global spend. However, despite being widely adopted by more than 20 million new cancer patients, imaging procedures are not capable of diagnosing and quantifying diseases in the initial stages of cancer progression. In addition, there is an unmet need for diagnostics that could minimise the need for surgical and biopsy procedures and identify molecular phenotype and tumours at early stages to reduce the chances of metastases. Introduction of non-invasive imaging-based tests for solid tumours will not only enable disease detection but also help in the diagnosis/quantification of cancerous cells in earlier stages of the disease, thereby providing Imagion's MagSense an edge over the currently employed imaging procedures.

Breast cancer – the leading 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 National Breast Cancer Foundation. On an 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. The growing number of patients with breast cancers is a significant addressable opportunity and we believe that the MagSense technology has the potential to capture a major proportion of the overall breast cancer diagnostics market.

Currently, mammograms[8] are typically used for screening or detection of breast cancers. According to MQSA National Statistics by the USFDA, each year, over 39.5 million mammograms are performed in the US (as of July 2019), translating into an annual spending of over US$10bn. Further, of the

[7] The unit of numbers on Y-axis is US$mn.
[8] Mammogram is an X-ray picture of the breast, which is captured to check for breast cancer in women.

total 39.5 million patients, >50% women experience false-positive results at least once during a period of 10 years while undergoing annual mammography procedure; hence, they are required to undergo lymph node biopsy to confirm the diagnosis. This results in additional spend worth US$4bn each year. In addition to that, breast cancer is often not detected or gets detected at later stages, because mammograms are often unable to detect early-stage breast cancers, resulting in >500,000 global annual deaths that can be prevented if the disease is diagnosed in earlier stages. There is a huge difference between the survival prospects of patients diagnosed in early stages (99% chance of survival) versus late stages (24% chance of survival). Therefore, in order to prevent deaths due to metastases of breast cancer, there is a need for a diagnostic technology that can accurately detect, as well as diagnose, disease in earlier stages of cancer. Imagion's technology presents a solution to this challenge by allowing early detection and continuous monitoring of disease progression.

Prostate cancer – a long-term market opportunity for Imagion

Prostate cancer, which represents the second most common cause of deaths among men (according to American Cancer Society) and acts as a major health threat across the globe, is also another type of cancer being targeted by the MagSense technology. Prostate cancer, which is diagnosed in about one in nine men during their lifetime, results in one death out of 39 men. According to GLOBOCAN 2018 estimates, the disease affected >1.3 million new patients in 2018 globally – representing a large patient population that can be captured by screening-cum-diagnostic test being developed by Imagion.

Prostate cancer, the second most common cause of deaths in men, is another indication being targeted by Imagion

Currently, prostate biopsy is the most common procedure for the diagnosis of the disease[9], although in some markets such as Australia the standard is PSMA PET imaging. In the US In the US alone, an annual spending of US$4.4bn is incurred to detect, screen and diagnose prostate cancer. However, despite the huge spending, the disease metastasises in 28% of the cases[10]. Therefore, there is need for a screening-cum-diagnostic tool that is more accurate and affordable for the screening or diagnosis of life-threatening prostate cancer. We believe that the MagSense technology has the potential to address these needs in the medium-to-long-term future. In markets where medical practice has already dropped biopsy, MagSense will be competing with a non-radioactive approach, however we believe the technology still has competitive advantage, most notably cost.

Ovarian cancer is another indication targeted by Imagion

Besides breast cancer, ovarian cancer is an indication being targeted by Imagion. The disease affects more than 22,530 US women every year and kills approximately 13,980 among them, as per 2018 estimates by the American Cancer Society. As per GLOBOCAN 2018 estimates, over 300,000 new cases of the disease were registered globally in 2018. 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. The MagSense technology has the potential to target this unmet need for procedures/screening tools that could detect ovarian cancer at earlier stages and increase the survival prospects of patients.

[9] Cancer. 2018 Jul 1;124(13):2733-2739. Epub 2018 May 21.
[10] In case the disease is not detected in earlier stages.

Currently, transvaginal ultrasound (TVUS) and the CA-125 blood test are commonly used tests for ovarian cancer screening; however, these tests have their own limitations. For instance, TVUS, which uses sound waves to search for tumours in ovaries, is incapable of distinguishing between cancerous and benign tumours and has very poor sensitivity, only detecting the tumor at late stage when very large. Similarly, the CA-125 test is less effective as a screening tool, as many other conditions that are unrelated to ovarian cancer could produce high CA-125 levels. 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$0.35bn in revenue, assuming all new ovarian cancer cases (~239,000) adopt Imagion's technology.

Valuing Imagion Biosystem

We value Imagion at 12 cents per share base case and 26 cents per share optimistic case, using a DCF-based approach. We assumed that the company did not partner MagSense but chose to build its own distribution system for the product. Our main assumptions were:

- **WACC:** ~13.6%, appropriate in our view for a 'Speculative' risk rating[11];
- **Probability of clinical success.** Thanks to MagSense's Breaklthrough Device status the regulatory hurdles for commercialising MagSense are fairly low. However, to account for the potential for any regulatory requirements that may slow CE Mark and 510(k) approval from the FDA we weighted our DCF by 90%;
- **Time horizon**. We used a 15-year time horizon in our DCFs followed by a terminal value;
- **Clinical costs.** We assume that a further A$8-15m is required to complete MagSense commercialisation;
- **Launch date.** We modelled a commercial launch in 2022 (optimistic case) or 2023 (base case).
- **Peak sales.** We assumed peak sales for MagSense of ~US$190m (base case) to US$240m (optimistic case). That this is reasonable is suggested by the current commercial experience of Foundation Medicine and similar companies[12].
- **Margins**. We assume 50-66% gross margins for MagSense from 2018/2019, alongside SG&A expenses equal to 10-20% of sales. We assume both COGS and SG&A decline by 0.1%-0.2% of revenue annually.
- **Currency:** While Imagion reports its numbers in Singapore dollars, we translated for valuation purposes a US$ revenue stream back into AUD$ at a long-run exchange rate for the AUDUSD of 0.7.
- **Tax:** We assumed a 30% tax rate.
- **Corporate overhead.** We assumed the equivalent of A$0.5m per month in corporate overhead going forward.
- **Further capital.** We assume A$20m in further capital needs to be raised in order to fully fund the global roll-out of MagSense. Purely for valuation purposes we use 4 cents per share as the average price at which this capital is raised.

[11] For a relevant discount rate, we use WACCs of between ~11% and ~15% depending on the risk for Life Science companies. This is derived from a RFR of 1.0%; a MRP of 7.5%-11.5% (7.5% for 'medium risk' companies, 9.5% for 'high risk' companies and 11.5% for 'speculative' companies); and an ungeared beta of 1.1. We regard Life Science companies with existing businesses, or who have enough capital to reach the market with their products, as 'Medium' risk. Companies that have small revenue streams from marketed products but that are still potentially in need of capital are 'High' risk. Everything else is 'Speculative'.

[12] In 2017 Foundation Medicine enjoyed US$152.9m in revenue, up 31% on 2016, with over 67,000 clinical tests performed during the year.

Figure 6: Our valuation of Imagion Biosystems

	Base	Optim.
MagSense (A$m)	91.9	215.3
Value of tax losses	9.7	9.7
Underlying R&D cost	-24.0	-24.0
Cash now (A$m)	1.1	1.1
Cash from options and cash to be raised (A$m)	22.8	22.8
Total value (A$m)	101.5	225.0
Total diluted shares (million)	877.5	877.5
Value per share	$0.12	$0.26
Valuation midpoint	$0.19	
Share price now (A$ per share)	$0.039	
Upside to midpoint	377.0%	

Source: Pitt Street Research

Re-rating Imagion Biosystems

We see the following factors contributing to the re-rating of Imagion in the direction of our valuation range:

- Successful completion of its first-in-human study in patients with HER2-positive breast cancer.
- Positive 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.

Imagion Biosystems has a strong management team

Robert Proulx, the current acting Chairman and CEO, has been associated with Imagion from the time when the company was the subsidiary of Manhattan Scientific. Robert brings over 25 years of experience in the life sciences and medical devices sectors. Within these sectors, he holds significant experience of working in sales management and marketing roles. Prior to joining Imagion, he served as the President and GM at Silicon Biosystems, a company that developed an image-based liquid biopsy diagnostic platform for circulating tumour cells.

Brian Conn, CFO, has been associated with Imagion since July 2016. He brings with him over 12 years of experience (within and outside the life sciences industry) of working as a finance executive across high-growth companies. Between 2011 and 2016, Brian served as CFO for a US-based industrial biotechnology company, Verdezyne, wherein he played a critical role in raising US$170m in equity, debt, project finance and government incentives. Prior to Verdezyne, he held executive positions, including CFO, at companies such as Chemicon International, Serologicals Corporation, Millipore Corporation and MicroIslet.

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. Her previous assignments include protein chemistry leadership at Dart Neuroscience, co-founder and COO at MicroStem, Senior Scientist at SGX Pharmaceutical (acquired by Lilly) and Research Scientist at 3DP (acquired by Johnson & Johnson).

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. He has been a chamopion of the MagSense technology at M.D. Anderson Cancer Center where he works in the Division of Diagnostic Imaging of the Department of Imaging Physics.

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. As the Global Technology Leader at GE, he led research for technologies such as X-ray, CT, MRI, ultrasound, nuclear medicine, PET and optical imaging.
- **Jovanka Naumoska**, Non-Executive Director and Corporate Secretary, is an Australian legal practitioner with significant experience in IP law, corporate law and corporate governance. She is also the Officer of Corporate Secretary for the company. She serves Australian scientific development organisations as an expert on matters pertaining to corporate law, business operations, IP development and regulatory compliance.
- **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. Additionally, he holds ~15 years of experience in the diagnostics space – led numerous new product efforts from concept to market launch.
- **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. He co-founded an Australian company, Diagnostic Technology, wherein he was responsible for the development of technology platforms for mainstream healthcare use.

– **Bronwyn Le Grice**, Non-Executive Director, has been associated with Imagion since April 2018. She holds more than 15 years of experience in the healthcare and technology markets, spanning venture capital, capital raising and corporate governance for Australian listed companies and non-profit organisations.

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.

CA125 – A tumour marker indicates ovarian cancer.

Circulating tumour cells – Tumour cells that have detached from a primary tumour and circulate in the bloodstream.

DNA methylation – A process by which methyl groups are added to the DNA molecule.

Epigenetic – The study of heritable phenotype changes, which do not involve alterations in the DNA sequence.

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.

Josephson junction – Two superconductors separated by a non-superconducting material. The movement of electrons through the non-superconducting barrier allows powerful electronic circuits to be created, as well as, extremely sensitive magnetometers and voltmeters.

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.

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

Next-generation sequencing – A new method for sequencing genomes at high speed and low cost.

Nucleosomes – A fundamental unit of DNA packaging in eukaryotes, consisting of a segment of DNA wound in sequence around eight histone protein cores.

PSA – Prostate-Specific Antigen, a protein produced exclusively by prostate cells often used as a biomarker for prostate cancer.

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.

Superconductor – A material that can conduct electricity perfectly in a manner that the current never degrades or dissipates.

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

As of 24 June 2019	In million	% of fully diluted	Note
Ordinary shares	323.7	85.8%	
Performance rights	10.8	2.9%	
Unlisted options	43.0	11.4%	Exercise price 6.6 cents; average expiry date 21-May-2021
Fully diluted shares	**377.5**		

Source: Company

Appendix III – IP position

Imagion Biosystems' intellectual property derives from the following applications:

Cell detection using targeted nanoparticles and magnetic properties thereof, WO/2011/053435, priority date October 5, 2009, invented by Edward Flynn and Richard Larson[13].

This patent application covers a method for detection of a specific type of cells in a biological sample using magnetic nanoparticles. The magnetic nanoparticles are conjugated to a cell-specific binding molecule (e.g., antibodies). The specialised magnetic nanoparticles may be used to detect cancer cells in blood.

[13] This patent application has been granted in the US as Patent No. 7,309,316 in December 2007; as Patent No. 8,060,179 in November 2011; as Patent No. 8,118,754 in February 2012; as Patent No. 8,447,379 in May 2013; as Patent No. 8,999,650 in April 2015; and as Patent No. 9,964,469 in May 2018.

Detection, measurement, and imaging of cells such as cancer and other biologic substances using targeted nanoparticles and magnetic properties thereof, WO/2011/057146, priority date November 6, 2009, invented by Edward Flynn [14]

This application pertains to a magnetic device and method for detection of cancer cells in vivo. The device is equipped with SQUID sensors and atomic magnetometers that can detect nanoparticles in sub-nanogram quantities, and thus, help in early detection of cancers. Importantly, in February 2019 Imagion received US continuation-in-part from this patent family (No. 10,194,825) to include treatment.

Methods and apparatuses related to magnetic relaxometry measurements in the presence of environmental response to magnetic excitation, WO/2018/187217, priority date April 2, 2017, invented by Todor Karaulanov and Giulio Paciotti.

This application pertains to an improved magnetic device for detection of a specific type of cells in a biological sample. The device is equipped with overcompensating coils, which suppress the generation of eddy currents and help mitigate the signal noise generated by the environment in response to magnetic pulses.

Synthesis of metal carboxylate compounds, WO/2015/187544, priority date June 2, 2014, invented by Erika Vreeland, Dale Huber, Gretchen Schober, and Andrew Price.

This application covers a method to produce anhydrous metal carboxylates, such as iron oleate (a raw material for production of magnetic nanoparticles) in an air- and water-free atmosphere. The carboxylates offer a uniform geometry and help maintain the size of magnetic nanoparticles produced across batches.

Viscosity measuring method, US/2012/0234080, priority date March 1, 2011, invented by Natalie Adolphi, Edward Flynn, Howard Bryant, and Kimberly Butler.

This application pertains to the use of specialised magnetic nanoparticles for determining the viscosity of a fluid. The diameters of the nanoparticles are selected and can be manipulated to eliminate errors due to adverse Neel relaxation effects.

Magnetic Relaxometry to Assess Disease via Circulating Markers, US/2016/0124063, priority date October 29, 2014, invented by Gerald Grafe.

This application covers a method for detection of a specific type of cells in a patient's circulatory system using magnetic nanoparticles. The method employs nanoparticles, which are conjugated to a cell-specific binding molecule (e.g., antibodies) and can be detected using a magnetic measurement system placed close to the body of the patient.

Methods and apparatuses related to instrumentation for magnetic relaxometry measurement, US/2015/0369887, priority date June 19, 2014, invented by Erika Vreeland, Dale Huber, Gretchen Schober, and Andrew Price.

This application covers magnetic gradiometers constructed using multiple atomic magnetometers. The magnetometers are placed at different distances

[14] This patent application has been granted in the US as Patent No. 9,074,976 in July 2015; as Patent No. 9,095,270 in August 2015; and as Patent No. 10,194,825 in February 2019.

from a sample, and their readings are recorded and analysed to measure a magnetic gradient.

Appendix IV – Papers relevant to Imagion Biosystems

Flynn and Bryant (2005), *A biomagnetic system for in vivo cancer imaging.* Phys Med Biol. 2005 Mar 21;50(6):1273-93. Epub 2005 Mar 2.

This paper describes procedures and parameters required for the implementation of an in vivo detection system using antibody-labelled magnetic nanoparticles. It also highlights methods of determining properties of magnetic nanoparticles. Additionally, it discusses the weak field magnetic sensor SQUID system and methodology of generating the magnetic polarisation pulse in order to align the magnetic moments of nanoparticles.

Serda et. al. (2007), *Targeting and cellular trafficking of magnetic nanoparticles for prostate cancer imaging.* Mol Imaging. 2007 Jul-Aug;6(4):277-88.

This research publication highlights the use of antibody-conjugated iron-oxide nanoparticles as a specific and sensitive tool for enhancing magnetic resonance (MR) images of both local and metastatic cancers. In this study, biotinylated anti-PSMA antibody conjugated with streptavidin-labelled iron oxide nanoparticles is used in MR imaging and confocal laser scanning microscopic imaging studies using LNCaP prostate cancer cell. The findings of the study showed enhancements in MR images with the use of PSMA for targeting prostate cancer cells.

McGill et. al. (2009), *Magnetically responsive nanoparticles for drug delivery applications using low magnetic field strengths.* IEEE Trans Nanobioscience. 2009 Mar;8(1):33-42. Epub 2009 Mar 16.

The paper highlights the potential of magnetic nanoparticles in enhancing drug delivery using a low oscillating magnetic field (OMF). The research work assessed the ability of magnetic nanoparticles to cause disruption of a viscous biopolymer barrier to drug delivery and the potential to induce triggered release of drug conjugated to the surfaces of these particles.

Jaetao et. al. (2009), *Enhanced leukaemia cell detection using a novel magnetic needle and nanoparticles.* Cancer Res. 2009 Nov 1;69(21):8310-6. Epub 2009 Oct 6.

This publication discusses a novel apparatus that uses antibodies conjugated to superparamagnetic iron-oxide nanoparticles (SPION) and directed against the acute leukaemia antigen CD34, coupled with a 'magnetic needle' biopsy for improving the detection of leukaemia cells in the marrow. Research results suggest that bone marrow biopsy via antigen-targeted magnetic nanoparticles and a magnetic needle for the evaluation of minimal residual disease in CD34-positive acute leukaemia could significantly enhance sensitivity versus the current standard of care.

Adolphi et. al. (2009), *Characterisation of magnetite nanoparticles for SQUID-relaxometry and magnetic needle biopsy.* J Magn Mater. 2009 May 1;321(10):1459-1464.

This study highlights the results from the characterisation of magnetite nanoparticles for SQUID-relaxometry and magnetic needle biopsy using methods such as SQUID-relaxometry, susceptometry and TEM.

Adolphi et. al. (2012), *Characterisation of single-core magnetite nanoparticles for magnetic imaging by SQUID relaxometry.* Phys Med Biol. 2010 Oct 7;55(19):5985-6003. Epub 2010 Sep 21.

In this study, the optimum particle size, single-core magnetite nanoparticles (with nominal average diameters 20, 25, 30 and 35 nm) were characterised using SQUID relaxometry, transmission electron microscopy, SQUID susceptometry, dynamic light scattering and zeta potential analysis.

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.

Wiekhorst et. al. (2012), *Magnetorelaxometry assisting biomedical applications of magnetic nanoparticles.* Pharm Res. 2012 May;29(5):1189-202.Epub 2011 Dec 8.

This article describes some applications of magnetorelaxometry (MRX) in cellular iron-oxide magnetic nanoparticles (MNP) quantification, MNP organ distribution and MNP-based binding assays. It reported MRX as a valuable tool for improving the application of MNP for diagnostic and therapeutic purposes.

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.

Johnson et. al. (2012), *Magnetic Relaxometry with an Atomic Magnetometer and SQUID Sensors on Targeted Cancer Cells.* J Magn 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.

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.

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.

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.

Appendix V – Major shareholders

The four major shareholders in Imagion include the following:

- Manhattan Scientifics, a publicly traded US technology developer that worked on MagSense technology between 2011 and 2016 (19.8%).
- Kemper Shaw, a Sydney investor (9.8%).
- Drake Special Situations, a US fund (7.7%).
- William Taylor Nominees Pty Ltd, an Australian private company (6.7%).

Appendix VI – Companies to watch

Company	Location	Code	Market cap (US$m)	Website
Immunovia	Lund, Sweden	Nasdaq OMX Stockholm: IMMNOV	310	www.immunovia.com
VolitionRx	Namur, Belgium	NYSE MKT: VNRX	200	www.volitionrx.com
Celcuity	Minneapolis, Mn.	Nasdaq: CELC	188	www.celcuity.com
ANGLE plc	Guildford, UK	LSE: AGL	178	www.angleplc.com
OncoCyte	Alameda, Ca.	NYSE MKT: OCX	115	www.oncocyte.com
MDxHealth	Herstal, Belgium	Euronext Brussels: MDXH	63	www.mdxhealth.com
Epigenomics	Berlin, Germany	Xetra: ECX	59	www.epigenomics.com
Imagion Biosystems	San Diego, CA	ASX:IBX	9	www.imagionbiosystems.com

Source: Pitt Street Research

ANGLE plc. This company's Parsortix technology allows viable circulating tumour cells to be sourced from blood samples. Having whole cells means that analysis can be made of DNA, RNA and proteins, which is a big step forward from only having circulating tumour DNA to analyse. Parsortix is CE marked as a tool for sourcing CTCs, and ANGLE is seeking FDA approval for its use in the diagnosis of metastatic breast cancer as an alternative to tissue biopsy.

Celcuity. This company's CELx platform uses cultured cells from patient tumours and analyses them for the activity of various aberrant signalling pathways indicative of cancer. This helps ensure that patients receive the right targeted therapies for such pathways. The company's first test from this platform was the CELx 'Multi-Pathway Signaling Function Test' for breast cancer, which measures various cellular signalling activity including HER2 in a patient's live tumour cells.

Epigenomics. This company's technology allows liquid biopsy of cancer through detection of DNA methylation biomarkers. Currently, the company has DNA methylation-based diagnostics on the market for colon and lung cancer.

Immunovia. This company's IMMray technology is an antibody microarray platform that can detect cancer from a blood test by surveying the various immunoregulatory proteins that would be associated with it. The company's first commercial test is PanCan-d for the early detection of pancreatic cancer. Immunovia is working on tests for other cancers and autoimmune diseases.

MDxHealth. This company's ConfirmMDx product is a test for the DNA methylation status of three prostate cancer genes, which can detect cancer from its 'epigenetic' profile, even if the original biopsy did not directly sample the cancerous tissue. The product reduces the need for repeat biopsies, for

which the standard PSA test is still high. SelectMDx is a similar product to ConfirmMDx which allows selection of high-risk patients for biopsy, allowing lower-risk patients to avoid it.

OncoCyte. This company's technology uses gene expression patterns associated with embryonic stem cell development to search for cancer genes in cancer tissues obtained from the blood or urine. A confirmatory lung cancer diagnostic called DetermaVu has reached the commercial launch stage.

VolitionRx. This company's technology allows the DNA signature of cancer to be detected in circulating nucleosomes, i.e., DNA wrapped around a protein core called a histone. A suite of diagnostics called 'Nu.Q' is being launched, starting with a colorectal cancer diagnostic.

Appendix VI – Risks related to Imagion

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

- **Funding risk**. More capital will likely be needed to continue clinical and -commercial development of MagSense.
- **Engineering risk**. There is the risk that the device currently being developed by Planet Innovation will take longer than expected to perfect.
- **Clinical risk**. There is the risk that Imagion's clinical work with MagSense will yield equivocal results
- **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.

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 Imagion.

Appendix VII – Analyst qualifications

Stuart Roberts, lead analyst on this report, has been covering the Life Sciences sector as an analyst since 2002.

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

General advice warning, Disclaimer & Disclosures

Terms & Conditions

The information contained herein ("Content") has been prepared and issued by Pitt Street Research Pty Ltd ACN 626365615 ("Pitt Street Research"), an Authorised Representative (no: 1265112) of BR Securities Australia Pty Ltd. ABN 92 168 734 530, AFSL 456663. All intellectual property relating to the Content vests with Pitt Street Research unless otherwise noted.

Disclaimer

The Content is provided on an as-is basis, without warranty (express or implied). Whilst the Content has been prepared with all reasonable care from sources we believe to be reliable, no responsibility or liability shall be accepted by Pitt Street Research for any errors, omissions or misstatements howsoever caused. Any opinions, forecasts or recommendations reflect our judgement and assumptions at the date of publication and may change without notice. Pitt Street Research will not accept any responsibility for updating any advice, views, opinions or recommendations contained in this document.

No guarantees or warranties regarding accuracy, completeness or fitness for purpose are provided by Pitt Street Research, and under no circumstances will any of Pitt Street Research officers, representatives, associates or agents be liable for any loss or damage, whether direct, incidental or consequential, caused by reliance on or use of the Content. History may not repeat. Portfolios need to be diversified.

General Advice Warning

The Content has been prepared for general information purposes only and is not (and cannot be construed or relied upon as) personal advice nor as an offer to buy/sell/subscribe to any of the financial products mentioned herein. No investment objectives, financial circumstances or needs of any individual have been taken into consideration in the preparation of the Content.

Financial products are complex, entail risk of loss, may rise and fall, and are impacted by a range of market and economic factors, and you should always obtain professional advice to ensure trading or investing in such products is suitable for your circumstances; ensure you obtain, read and understand any applicable offer document.

Disclosures

Pitt Street Research has been commissioned to prepare the Content. From time to time, Pitt Street Research representatives or associates may hold interests, transact or hold directorships in, or perform paid services for, companies mentioned herein. Pitt Street Research and its associates, officers, directors and employees, may, from time to time hold securities in the companies referred to herein and may trade in those securities as principal, and in a manner which may be contrary to recommendations mentioned in this document.

Pitt Street Research receives fees from the company referred to in this document, for research services and other financial services or advice we may provide to that company. The analyst has received assistance from the company in preparing this document. The company has provided the analyst with communication with senior management and information on the company and industry. As part of due diligence, the analyst has independently and critically reviewed the assistance and information provided by the company to form the opinions expressed in the report. Diligent care has been taken by the analyst to maintain an honest and fair objectivity in writing this report and making the recommendation. Where Pitt Street Research has been commissioned to prepare Content and receives fees for its preparation, please note that NO part of the fee, compensation or employee remuneration paid will either directly or indirectly impact the Content provided.