INOVIQ Limited

IIQ.ASX

A research platform of MST Financial

7 July 2023

Global Joint Marketing Agreement: Major Boost to EXO-NET® Profile

NEED TO KNOW

- IIQ signs a joint marketing agreement with leading global biotechnology company, Promega Corporation
- Both partners anticipate expansion of the agreement
- Exosome market expected to reach US$8.7b by 2029

Promega agreement introduces EXO-NET® technology to a broad global customer base: INOVIQ (IIQ) and Promega Corporation (Promega) sign a global joint marketing agreement for INOVIQ's EXO-NET® exosome capture technology and Promega Nucleic Acid purification systems worldwide. Promega is a global leader in the manufacturer of enzymes and other products for biotechnology and molecular biology with reported FY22 revenue of over US$700m. The company is headquartered in Madison, WI, USA with branches in 16 countries and over 50 global distributors. Promega's portfolio of over 4,000 products supports a range of life science work and is used by researchers in academic institutions, pharmaceutical companies, clinical diagnostics laboratories, and other life science organizations worldwide.

Agreement expected to expand beyond co-marketing: Under the agreement global customers of Promega will be offered a wide range of Promega manual and automated nucleic acid extraction reagents and instruments combined with INOVIQ's EXO-NET exosome capture tools. The initial term of the agreement is three years, with one-year automatic renewals unless terminated by either party. Both partners expect the agreement will expand to cover a range of exosome solutions for exosome isolation, characterisation, and analysis kits.

Target market expected to reach US$8.7b by 2029: The market for exosome isolation, biomarker discovery and diagnostics research applications is expected to reach US$8.7b by 2029.

Investment Thesis

Diversified portfolio of versatile technology platforms and products: IIQ's portfolio is wide, with its EXO-NET and SubB2M technologies creating substantial new opportunities alongside its existing hTERT test, as well as potential future royalties from BARD1.

Collaboration with UQ to develop ovarian cancer screening test based on EXO-NET technology: This collaboration combines best-in-class exosome capture technology with University of Queensland (UQ) biomarkers for application in liquid biopsies.

SubB2M platform: strong data in ovarian, breast cancers support potential to supercharge current tests and monitor disease progression: The company expects that the SubB2M-CA15-3 breast cancer test could be market-ready for a lab partner from December 2023.

Valuation

We value IIQ at A$213m or A$2.31 per share, using a risk-adjusted net present value (rNPV) method to discount future cash flows through to 2043, consistent with the expiry life of patent families.

Risk

Key risks to our valuation include demonstrating efficacy, establishing clinical utility, and meeting regulatory requirements (see '*Sensitivities and Risks*').

Equities Research Australia

Pharmaceuticals, Biotechnology and Life Sciences

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INOVIQ is developing and commercialising next-generation exosome solutions and precision diagnostics to improve the diagnosis and treatment of cancer and other diseases. The company has commercialised the EXO-NET pan-exosome capture tool for research purposes and the hTERT test as an adjunct to urine cytology testing for bladder cancer. Its cancer diagnostic pipeline includes blood tests in development for earlier detection and monitoring of ovarian, breast and other cancers.

https://www.inoviq.com/

Valuation	**A$2.31** *(unchanged)*
Current price	**A$0.94**
Market cap	**A$86m**
Cash on hand	**A$8.8m** *(31 March 2023)*

Upcoming Catalysts/Newsflow

Period	
1QFY24	EXO-NET partnering progress
1QFY24	SubB2M SPR feasibility data
1HFY24	SubB2M/CA125 OC test: analytical data
2QFY24	SubB2M/CA15-3 test: monitoring study data

Share Price (A$)

Source: FactSet, MST Access.

INOVIQ LTD IIQ

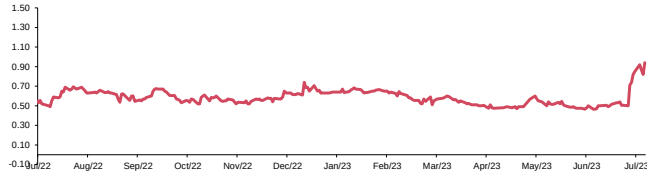
IIQ-AU

Year end 30 June, AUD unless otherwise noted

MARKET DATA

Price	**$**	**0.94**
52 week high / low	$	0.47-0.94
Valuation	**$**	**2.31**
Market capitalisation	$m	86.5
Shares on issue (basic)	**m**	92.0
Options / rights	m	9.3
Other equity	m	0.0
Shares on issue (diluted)	**m**	**101.4**

12-MONTH SHARE PRICE PERFORMANCE (A$)



INVESTMENT FUNDAMENTALS		FY21A	FY22A	FY23E	FY24E	FY25E
Reported NPAT	$m	(11.2)	(18.2)	(9.8)	(9.1)	(5.5)
Underlying NPAT	**$m**	**(11.2)**	**(18.2)**	**(9.8)**	**(9.1)**	**(5.5)**
Reported EPS (diluted)	¢	(14.4)	(20.0)	(10.7)	(9.9)	(5.0)
Underlying EPS (diluted)	**¢**	**(14.4)**	**(20.0)**	**(10.7)**	**(9.9)**	**(5.0)**
Growth	%					
Underlying PER	x	**nm**	**nm**	**nm**	**nm**	**nm**
Operating cash flow per share	¢	(5.7)	(6.6)	(7.9)	(6.9)	(3.5)
Free cash flow per share	¢	(2.5)	(7.0)	(8.2)	(7.4)	(3.5)
Price to free cash flow per share	**x**	**nm**	**nm**	**nm**	**nm**	**nm**
FCF Yield	%	nm	nm	nm	nm	nm
Dividend	**¢**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Payout	%	0.0%	0.0%	0.0%	0.0%	0.0%
Yield	**%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**
Franking	%	0.0%	0.0%	0.0%	0.0%	0.0%
Enterprise value	**$m**	**82.8**	**72.1**	**79.7**	**77.9**	**77.2**
EV/EBITDA	x	(6.3)	(4.0)	(9.4)	(10.1)	(18.1)
EV/EBIT	x	(5.9)	(3.6)	(8.1)	(8.5)	(13.9)
Price to book (NAV)	x	3.0	3.1	4.5	5.2	5.8
Price to NTA	x	29.7	5.2	9.7	9.6	10.0

KEY RATIOS		FY21A	FY22A	FY23E	FY24E	FY25E
EBITDA margin	%	nm	nm	nm	nm	nm
EBIT margin	%	nm	nm	nm	nm	nm
NPAT margin	%	nm	nm	nm	nm	nm
ROE	%	nm	nm	nm	nm	nm
ROA	%	nm	nm	nm	nm	nm
Net tangible assets per share	$	0.0	0.2	0.1	0.1	0.1
Book value per share	$	0.3	0.3	0.2	0.2	0.2
Net debt/(cash)	$m	(3.7)	(14.4)	(6.8)	(8.6)	(9.3)
Interest cover/ (EBIT/net interest)	x	nm	nm	nm	nm	nm
Gearing (net debt/EBITDA)	x	nm	nm	nm	nm	nm
Leverage (net debt/(net debt + equity))	x	nm	nm	nm	nm	nm

DUPONT ANALYSIS		FY21A	FY22A	FY23E	FY24E	FY25E
Net Profit Margin	%	nm	nm	nm	nm	nm
Asset Turnover	x	0.0	0.0	0.0	0.1	0.3
Return on Assets	%	nm	nm	nm	nm	nm
Leverage	x	1.2	1.1	1.1	1.1	1.1
Return on Equity	%	nm	nm	nm	nm	nm

KEY PERFORMANCE INDICATORS	FY21A	FY22A	FY23E	FY24E	FY25E
SubB2M			0.0	0.0	0.2
SubB2M			0.0	0.2	1.9
EXO-NET Research Use Only			0.1	1.1	3.9
EXO-NET DX (Clinical)			0.0	0.0	0.0
hTert	0.5	0.28	0.3	0.3	0.3

HALF YEARLY DATA		2H21	1H22	2H22	1H23	2H23
Product revenue	$m	0.3	0.1	0.2	0.2	0.1
Operating expenses	$m	(11.9)	(4.4)	(17.9)	(6.3)	(4.8)
EBITDA	$m	(9.9)	(3.3)	(14.9)	(5.6)	(4.3)
EBIT	$m	(10.8)	(3.3)	(17.0)	(5.6)	(4.3)
PBT	$m	(10.8)	(3.3)	(17.0)	(5.6)	(4.3)
Reported NPAT	$m	(7.9)	(2.7)	(15.5)	(5.6)	(4.3)

PROFIT AND LOSS		FY21A	FY22A	FY23E	FY24E	FY25E
Product revenue	**$m**	**0.5**	**0.3**	**0.4**	**1.6**	**6.4**
income	$m	**1.0**	**1.8**	**1.0**	**0.9**	**1.2**
Operating expenses	$m	(15.5)	(22.3)	(11.2)	(11.2)	(11.3)
EBITDA	**$m**	**(13.1)**	**(18.2)**	**(8.4)**	**(7.7)**	**(4.3)**
Depreciation & Amortisation	$m	(0.9)	(2.1)	(1.4)	(1.4)	(1.3)
EBIT	**$m**	**(14.0)**	**(20.3)**	**(9.8)**	**(9.1)**	**(5.5)**
Interest expense	$m	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)
Pretax Profit	$m	(14.0)	(20.3)	(9.8)	(9.1)	(5.5)
Tax expense	$m	2.9	2.1	0.0	0.0	0.0
Reported NPAT	**$m**	**(11.2)**	**(18.2)**	**(9.8)**	**(9.1)**	**(5.5)**
Weighted average diluted shares	m	92.0	92.0	92.0	111.6	121.4

GROWTH PROFILE		FY21A	FY22A	FY23E	FY24E	FY25E
Revenue	%	nm	(40.9)	5.0	5.0	5.0
EBITDA	%	303.1	38.4	(53.5)	(8.1)	(44.9)
EBIT	%	331.1	44.4	(51.6)	(7.1)	(39.3)
Reported NPAT	%	242.7	63.2	(46.1)	(7.1)	(39.3)

BALANCE SHEET		FY21A	FY22A	FY23E	FY24E	FY25E
Cash	$m	5.0	15.4	7.8	9.6	10.3
Receivables	$m	0.2	1.7	0.2	0.2	0.2
Other	$m	0.4	0.4	0.4	0.4	0.4
Current assets	**$m**	**5.6**	**17.5**	**8.4**	**10.2**	**10.9**
PPE	$m	0.6	0.8	1.0	1.4	1.3
Intangible assets	$m	15.1	11.7	10.5	9.3	8.3
Goodwill	$m	11.0	0.0	0.0	0.0	0.0
Other	$m	1.1	0.9	1.7	1.6	1.5
Non current assets	**$m**	**27.9**	**13.3**	**13.2**	**12.3**	**11.1**
Total assets	**$m**	**33.5**	**30.8**	**21.6**	**22.5**	**22.0**
Trade and other payables	$m	0.8	1.0	0.8	0.8	0.8
Lease liabilities	$m	0.3	0.4	0.4	0.4	0.4
Other	$m	0.4	0.4	0.4	0.4	0.4
Current liabilities	**$m**	**1.5**	**1.8**	**1.5**	**1.5**	**1.5**
Lease liabilities	$m	0.9	0.6	0.6	0.6	0.6
Other liability	$m	2.1	0.0	0.0	0.0	0.0
Non current liabilities	**$m**	**3.0**	**0.7**	**0.7**	**0.7**	**0.7**
Total liabilities	**$m**	**4.5**	**2.5**	**2.2**	**2.2**	**2.2**
Net assets	**$m**	**29.1**	**28.3**	**19.4**	**20.3**	**19.8**
Share capital	$m	51.8	69.1	70.3	80.3	85.3
Retained earnings	$m	(24.0)	(41.9)	(52.0)	(61.1)	(66.6)
Other	$m	1.2	1.1	1.1	1.1	1.1
Total equity	**$m**	**29.1**	**28.3**	**19.4**	**20.3**	**19.8**

CASH FLOW		FY21A	FY22A	FY23E	FY24E	FY25E
Net loss for period	**$m**	**(11.2)**	**(18.2)**	**(9.8)**	**(9.1)**	**(5.5)**
Depreciation & Amortisation	$m	(0.9)	(2.1)	(1.4)	(1.4)	(1.3)
Changes in working capital	$m	(0.4)	(1.1)	1.2	0.0	0.0
Other	$m	7.2	15.3	2.7	2.7	2.5
Operating cash flow	**$m**	**(5.3)**	**(6.1)**	**(7.3)**	**(7.7)**	**(4.3)**
Payments for PPE	$m	(0.8)	(0.4)	(0.3)	(0.5)	0.0
Other	$m	3.8	0.0	0.0	0.0	0.0
Investing cash flow	**$m**	**3.0**	**(0.4)**	**(0.3)**	**(0.5)**	**0.0**
Equity	$m	0.3	18.5	0.0	10.0	5.0
Lease liability payments	$m	(0.3)	(0.3)	0.0	0.0	0.0
Other	$m	0.0	(1.2)	0.0	0.0	0.0
Financing cash flow	**$m**	**(0.0)**	**16.9**	**0.0**	**10.0**	**5.0**
Cash year end	**$m**	**5.0**	**15.4**	**7.8**	**9.6**	**10.3**
Free cash flow	**$m**	**(2.3)**	**(6.5)**	**(7.6)**	**(8.2)**	**(4.3)**

Source: Company reports, MST Access estimates

INOVIQ's EXO-NET® Technology:
Thesis: Harnessing Power of Extracellular Vesicles

The Potential of EVs: Carriers of Biological 'Messages in a Bottle'

Extracellular vesicles (EVs) are lipid-bound vesicles which are released by all cell types, carrying precious cell-derived biomolecules, including nucleic acids (RNA and DNA), lipid, proteins, and metabolites. EVs are found in all biofluids and are involved in cell-to-cell communication and cell maintenance between local and distant cells. The delivery and uptake of their 'cargo' by other recipient cells facilitates both normal physiological and pathological (disease) processes in these other cells. EVs and their cargo represent valuable sources of critical information, with potential uses in both diagnostics (transport carriers of biomarkers) and therapeutics (optimising active cargo for drug delivery, and/or intrinsic properties related to cell of origin).

Exosomes – tiny carriers of biomolecular material have great potential, given their many roles as messengers of health and disease

Exosomes are a type of small EVs which are found in various body fluids and secreted by all cells in the body. Exosomes communicate with other cells and regulate their function. A specific inward budding formation process (see Appendix -'The science of exosomes') packages active cargo (proteins, nucleic acids, and lipids) from parent cells and delivers it to other neighbouring or distant cells and alters the function of recipient cells with cargo (e.g., healthy, or diseased) of instructions that are to be communicated to other cells. By capturing exosomes using EXO-NET, their molecular information can be used to identify changes in the cell's function and the early onset of diseases, including cancer.

The clinical utility of exosomes stems from their safety, biocompatibility, low immunogenicity, presence in most biofluids (plasma, serum, urine, saliva, semen, cerebral spinal fluid (CSF), breast milk, and amniotic fluid), ability to permeate tissue including the blood-brain barrier due to their small size, high biological stability, and different biological functions given different parent cells. Many varied biomolecules have been identified from exosomes (4,400 proteins, 194 lipids, 1,639 mRNAs, 764 miRNAs), highlighting the complexity of information carried and diversity of roles performed. These pathways can be used for diagnosis of disease or for therapeutic interventions, and the cargo carried by exosomes can be altered to deliver therapeutic agents.

Clinical applications of exosomes: research uses, disease identification (diagnostics) and treatment (therapeutics)

Diagnostics – Exosomes derived from different cell types have different functional characteristics given both their 'cargo' of specific proteins, lipids, and nucleic acids[1] and transmembrane proteins or nucleic acids of the exosome lipid membrane itself. As such, exosomes carry rich sources of information about their origin (parent) cell. This supports the use of exosome-based biomarker approaches to understand the underlying pathology of different types of parent cells (e.g., liver, ovaries, heart, blood, brain). Further, the composition of secreted exosomes can change as different pathologies progress, making the detection of variations valuable as diagnostic and prognostic biomarkers as well as potential therapeutic targets of disease. **Therapeutics –** Beyond diagnostics, exosomes have shown potential as drug delivery systems stemming from their capacity to deliver complex payloads. This, along with their ability to interact with and be taken up by target cells, has raised hopes of using exosomes as targeting carriers of therapeutic drugs.

The technical hurdles – why the potential of exosomes has not yet been fully realised and where EXO-NET provides a high-throughput solution

The two main hurdles to date for the clinical use of exosomes generally (and liquid biopsy techniques in particular) have been to efficiently: (1) **scale the extraction process** to ensure optimal and reproducible enrichment and yield for the reliable measurement of biomolecules of interest (e.g., tumour-derived exosomes); and (2) **separate exosomes of interest** from other EVs and biomolecules of similar size. This has led to a lack of standardisation, source heterogeneity and source matrix complexity and reproducibility. Various methods have been used over the past decade; however, no practical technology can currently isolate EVs completely from other non-EV components. Factors include the complexity of biological fluids; the considerable overlap of the physicochemical and biochemical properties among the exosomes, lipoproteins, virus, and other EVs; and the heterogeneity of exosomes themselves[2].

[1] Exosomes: biogenesis, biologic function, and clinical potential. Zhang et al (2019)

[2] Progress, opportunity, and perspective on exosome isolation - Efforts for efficient exosome-based theranostics: Yang et al (2020)

INOVIQ's EXO-NET® Technology – Overview

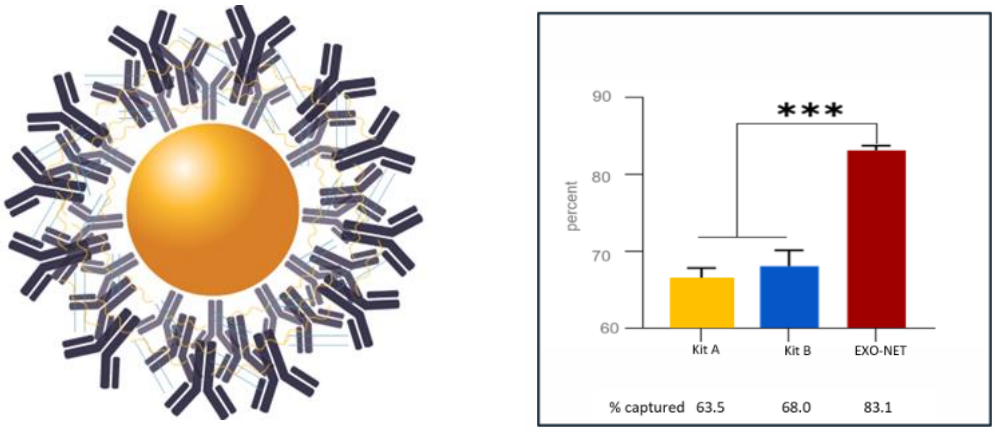
IIQ's EXO-NET® is a proprietary magnetic bead–based immunoaffinity capture technology for isolating EVs, including exosomes, from small clinical sample volumes of biofluids (plasma, urine, saliva, and cell-conditioned medium).

Innovative design – flexible, customisable, and compatible with other test formats

Magnetic bead–based capture of specific targets is a well-established and proven technology. However, IIQ has adapted this approach to build an exosome capture system, using a panel of monoclonal antibodies in a proprietary three-dimensional matrix (EXO-NET®) constructed on nanobeads (Figure 1).

Unlike other magnetic bead constructs using single layers of antibody molecules, EXO-NET® is composed of a collection of exosome-specific antibodies covalently linked to form a 3D multilayered antibody matrix. This matrix construct has been shown to increase binding avidity and analyte capture and outperform the more time-intensive ultra-centrifugation and size exclusion chromatography (SEC) methods, which to date have been considered the gold standard. EXO-NET captures 83.1% of small EVs (exosomes) from samples.

Figure 1: EXO-NET® technology: (conceptual schematic– left); EXO-NET captures 83.1% of small EVs (right)

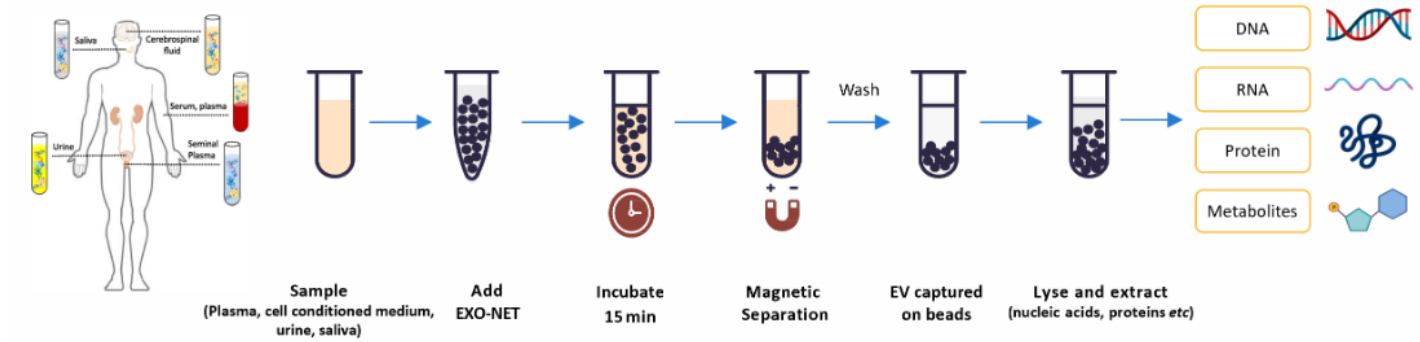


Source: INOVIQ. NB. Kit A and Kit B are two other bead-based EV isolation kits

How it works: EXO-NET® captures EV targets in 4 simple steps

The technology comprises a proprietary molecular matrix, made of antibodies, designed to capture targets of interest (wide range of EVs from different cell types), which is applied to magnetic beads (nanobeads). The use of the three-dimensional matrix increases the density and surface area occupied by the antibodies, thereby increasing the accessibility of ligand binding sites and extraction efficiency. The antibody matrix attached to these beads has been designed to capture a wide range of EVs from different cell types (Figure 2). IIQ can customise the mix of antibodies in the matrix to capture different types of exosomes.

Figure 2: EXO-NET® – workflow for exosome capture within 15 minutes



Source: INOVIQ.

The Competitive Advantages of EXO-NET®: Rapid, Efficient, Pure, Scalable

Immunomagnetic bead capture scores highly vs commonly used EV isolation techniques

The Endocrine Society Scientific Statement, published in 2022, reported that immunomagnetic bead capture approaches were found to outperform commonly used EV enrichment (isolation) techniques when assessed using the key features of:

- time: length of operation time
- cost: cost of the equipment and consumables
- scalability: the ease of scaling the technique to process large volumes of fluids
- recovery (yield): the percentage of EVs in fluids that could be extracted (yield)
- specificity: ratio of EVs extracted relative to total protein.

Figure 3: Comparison of the key features in commonly used extracellular vesicle enrichment techniques

EV enrichment techniques	Time	Cost	Scalability	Recovery	Specificity
PEG precipitation	+++	+++ +	++++	++++	+
Size exclusion chromatography	+	+	+	+	+++
High MW centrifugal filters	++++	+++	++++	+++	++
Differential ultracentrifugation	+	++	+	+	++
Tangential flow filtration	+++	++	++++	+++	+++
Affinity chromatography	++	+	++	++	++++
Immunomagnetic bead capture	++++	+++	++++	+++	++++

Source: Endocrine Reviews: Salomon et al (2022). (+ denotes the desirability of the feature, from +: least to ++++: most desirable).'NB. PEG = Polyethylene glycol precipitation

EXO-NET® technology advantages suggest it's a 'best-in-class' EV isolation system

Product features and major technological advantages of EXO-NET® include:

- rapid isolation of an enriched population of EVs from any biofluid (within 15–20 minutes)
- cost effective to use (avoiding time-consuming workflows of the current gold standard methods)
- scalable for high-throughput sample processing and can be fully automated
- flexible enough to be deployed on most lab test modalities (well plates, polymer beads, magnetic beads, and lateral flow devices)
- higher yield: recovery by isolating EVs results in higher yield of useful targets
- high purification of exosomes eliminating contaminants and reducing background noise
- simple (4 steps) and compatible with downstream testing formats (Mass Spec, RNA Seq etc for proteomic and RNA analysis)
- customisable: EXO-NET® is designed to capture a wide range of biological targets subject to proteins that are present on their surface being recognised by the capture ligands incorporated in the matrix (or NET) which can be adjusted

Good Manufacturing Practice (GMP) compliance also underpins competitive advantage

The ability to scale the process for high-throughput processing, combined with the time saved compared to other methods, supports high throughput requirements of most commercial laboratories. The company is in the process of converting its main lab in Australia to GMP[3] standards. As such, clinical and large-scale production of EXO-NET® under GMP-compliant standards would differentiate EXO-NET® and provide a clear competitive advantage for all future applications of the technology

[3] Good Manufacturing Practice (GMP) is a system for ensuring that products are consistently produced and controlled according to a set of prescribed quality standards.

Sensitivities and Risks

Demonstrating **efficacy in detection** of specified cancer and meeting **requirements of regulatory authorities** across different markets represent the two key risks for IIQ. Others are detailed below.

Technology Transfer

The success of IIQ's development programs rely on both the validation of the underlying mechanism of action/target of interest and the development of test formats (SPR, immunoassay) for measuring these targets. The development of various testing formats brings into question choice of reagents, antibodies other laboratory tools. This in effect represents a risk related both to technology and its transfer across testing formats.

Funding

In the absence of a development partner and with A$8.8m in cash (as at 31 March 2023), the potential need for funding remains high. Adding to funding requirements will be the choice of regulatory pathway (LDT, 510 (k), IDE) which in turn may require additional clinical trials to be conducted.

Competition

Targeting earlier detection of cancer remains an area of strong clinical interest and research development. Nonetheless, ovarian and breast cancers lack an early blood test detection standard which suggests there is room for new entrants.

Development and Commercialisation

New product development of IVDs rely on the translation of promising clinical data to date to testing formats that can be validated in retrospective trials using large blood sample banks (such as the UK ovarian cancer biobank). Further, for commercialisation of the tests IIQ will need to demonstrate the benefits of adding to current standards. Central to commercialisation of the SubB2M test will be the development of ELISA formats which are typically low-cost and commonly used in industry.

Regulatory Approval

Regulatory oversight of diagnostic tests Is fragmented. There are multiple frameworks under which diagnostic tests can seek regulatory approval.

As such the risks will be dependent on whether IIQ seeks FDA clearance or approval or alternatively under CLIA regulations enter the market as a LDT developed test. Notably, all IVDs (including LDTs and reagents) are categorised as medical devices, but the FDA has historically not exercised its regulatory authority with respect to LDTs. While the regulation of LDTs comes under CLIA regulation, the FDA has been pursuing control over LDTs for more than a decade, citing concerns over the level of rigour in validation and resultant safety in use.

Reimbursement

Reimbursement of the test may be a key determinant of its adoption and ultimate commercial success. This will be determined by ultimate cost and efficacy relative to current options.

Intellectual Property

A solid patent position represents a significant barrier to entry in medical technology. IIQ's current patent portfolio is expanding.

Appendix - The science of exosomes

Extracellular vesicles and exosomes – what are they, and what do they do? The term 'extracellular vesicle' was first coined in the 1970s to describe non-replicating semi-spherical vesicle structures secreted by cells into the extracellular space. EVs play an important role in the communication between cells in both healthy and disease settings. They have been found in all bodily fluids, including plasma, urine, milk, tears, sweat and semen, as well as in the plant kingdom and in micro-organisms.

EVs comprise a core containing a variety of cargoes such as nucleic acids, lipids and proteins associated with the cell's plasma membrane, encapsulated by a lipid bilayer membrane. EVs can be categorised by size – small and large, with exosomes being the smallest.

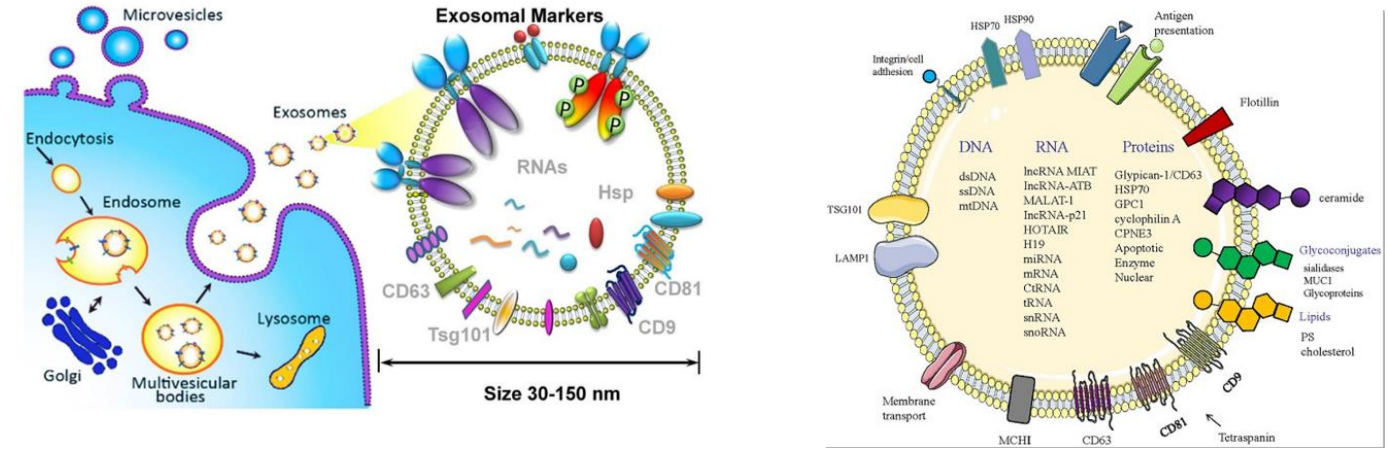
Figure 4: Relative sizes of EVs – exosomes are tiny (left); The formation of exosomes (right)

Source: Extracellular Vesicles and Their Emerging Roles as Cellular Messengers in Endocrinology: An Endocrine Society Scientific Statement, Salomon et al (2022).

How exosomes develop (biogenesis) and obtain their information-filled 'cargo'. Exosomes, a type of small EV, typically range from 30 to 150 nm in size. They are generated in several steps.

- The cell buds inward, creating a body called an 'endosome' inside the cell.
- Within the endosome, the internal budding process continues, filling it with tiny 'intraluminal vesicles'. As these vesicles are created, they are loaded with their 'cargo': nucleic acids (DNA, mRNA, miRNA), proteins and lipids.
- The loaded intraluminal vesicles are now called 'exosomes', and the endosome is now a 'multivesicular body' (MVB). The MVB, containing exosomes, is trafficked to the cell's plasma membrane. The MVB and plasma membrane fuse, releasing the exosomes with their cargo into the extracellular space (Figure 5).

Figure 5: Exosome biogenesis (formation), properties, and molecular composition



Source: Microfluidic Exosome Analysis toward Liquid Biopsy for Cancer; He et al (2016), https://www.jcancer.org/v12p5035.htm

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