



# Oncosil Medical Limited (OSL)

Speculative Buy

Initiating Coverage; Late Stage Pancreatic Cancer Focus to Bear Fruit

\$0.145

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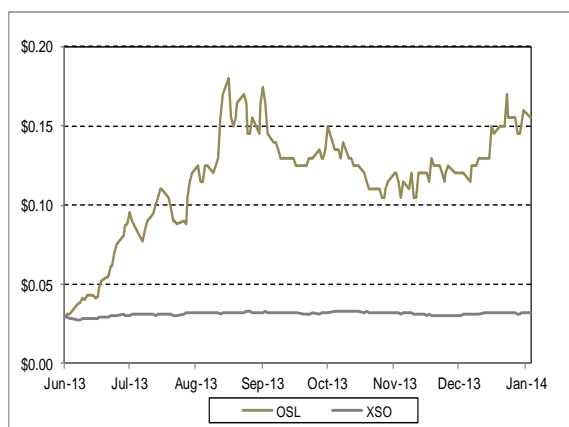
## Summary

Market cap (\$M)	\$45.0
Share price	\$0.145
Cash on Hand (31/12/13)	\$11.1m
52 week low	\$0.03
52 week high	\$0.18
Ave Monthly Vol (M)	17.2
Price Target	\$0.26

## Key Financials (A\$'000)

Year end June	FY13	FY14	FY15
	Actual	Estimate	Estimate
Revenue	88	105	339
SG&A	(857)	(986)	(1,055)
R&D	(130)	(850)	(2,007)
EBITDA	(981)	(1,732)	(2,729)
Reported NPAT	(881)	(1,627)	(2,390)
NPAT Adj.	(881)	(1,627)	(2,390)
EV/Sales	n/a	n/a	n/a
EV/EBITDA (x)	n/a	n/a	n/a
Reported PER (x)	n/a	n/a	n/a
ROE	-29.1%	-17.0%	-20.2%

## Share Price Graph (A\$)



## Key Points

Oncosil Medical (OSL) is a medical device company which is shortly to commence recruiting a major clinical study in inoperable pancreatic cancer.

Oncosil™ is a biocompatible silicon resin embedded with a radioisotope that is administered directly into pancreatic tumours by a gastroenterologist.

Oncosil™ remains embedded in the tumour and emits radiation over several weeks, thereby potentially controlling cancer growth and spread.

Potential for major impact in locally advanced pancreatic cancer (LAPC) in the medium term, given the large unmet medical need.

## Our View

- Loco-Regional Approaches to Managing Pancreatic Cancer are Lacking** – Current Standard of Care (SOC) in pancreatic cancer is the administration of two systemic chemotherapy agents, which show median overall survival (OS) of just 8.5 months (this has improved only ~2 months in last 18 years). We believe OSL will find clinician utilisation in early LAPC patients, where the cancer is confined to the pancreas (i.e. not metastatic). We think this market is approx 28,000 patients annually in the US, EU(7) and AUS. The aim of Oncosil™ will be to slow progression and increase OS, while also controlling pain and as a 1-2x procedure, significantly enhancing patient Quality of Life (QoL).
- Pilot Study Data was Promising** – A 17 patient (pt) study showed Oncosil™ + SOC chemotherapy (gemcitabine) delivered an impressive median OS of 10 mths and progression free survival (PFS) of 4 mths. Historic gemcitabine OS is ~6 mths and PFS 3.7 mths. Of the 17 patients recruited, six had locally advanced disease, 11 metastatic disease, which is an interesting outcome, albeit in a small number of patients.
- Design of Pivotal Study Crucial** – Intended design is for a 150 patient study (2:1 randomisation), with an interim analysis of PFS to determine futility and continuation. OSL has designated the study a pre-market approval (PMA) “support” study. We like the adaptability aspect envisaged – OSL should ramp up the number of pts post an interim analysis in our view to drive a 30% improvement in OS, the baseline improvement considered clinically significant. We believe the present trial is powered for a ~53% improvement in OS, reflecting the benefit from the pilot study. A larger study that provides increased power to detect a smaller OS benefit may be more advantageous than a small study with a non-significant outcome, which we think will require an additional study for efficacy to meet US regulatory requirements (PMA) for a class III medical device like Oncosil™. Recruitment is expected to take 12-18 mths, with interim analysis at ~12 mths examining PFS in 30 pts at >6 mths on study.
- Outlook** – Providing OSL leverages the innate flexibility in its design, based on the pilot studies and potentially a 15%+ interim PFS result, the product has sig. potential. We therefore initiate coverage with a Speculative Buy and 12 month PT of \$0.26. Risks include slower than expected clinical trial recruitment, clinical trial failure, incremental benefit to SOC limiting use, changes in pancreatic cancer SOC over time, improvements in external beam radiation approaches, reimbursement, clinician training and adoption.

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## Investment Thesis

**OncoSil Medical Limited (OncoSil, or ‘the Company’; ASX:OSL)** is an Australian based medical device company with a single lead product called **OncoSil™**, an implantable radioactive medical device used in the treatment of inoperable pancreatic cancer. The Company has completed several pilot studies in pancreatic cancer, which showed promise. The Company recently announced the commencement of its larger registration-directed trial.

As an investment case, we note several key facets to the **OSL** business model we find attractive:

1. **Unmet Medical Need in Pancreatic Cancer** – pancreatic cancer has one of the worst life expectancies of any cancer, given the late stage diagnosis. Typically one year survival rate is 26% and five year survival is 6%.
2. **Current Treatments Are Lacking** – the current standard of care (gemcitabine) was approved approx 18 years ago, with only one additional treatment approved that can be considered effective approved in late 2013 (Abraxane®). Despite this, the median overall survival has increased by ~2 months to 8.5 months over the period.
3. **External Beam Radiation in Combination with Chemotherapy Has Shown to Not Improve Survival Outcomes** – although controversial, a recent study highlighted that combining external radiation with chemotherapy did not improve survival outcomes v chemotherapy alone. External beam radiation is considered a standard of care, and does positively impact patient pain. A localised approach such as **OncoSil™** operating within the tumour may therefore be more synergistic.
4. **There is a Need to Increase Surgical Re-Section Rates in Locally Advanced Pancreatic Cancer (LAPC)** – while a newly diagnosed patient has a 15% of being eligible for surgery, one treatment goal for chemotherapy agents is to shrink pancreatic tumours to facilitate the down-staging of unresectable tumours to resectable. As a high dose intratumoral treatment modality, **OncoSil™** is well positioned to increase these rates.
5. **Pharmaceutical Interest is High** - two very significant license deals in pancreatic cancer over the last 18 months that collectively were worth over US\$1 billion in upfront and milestone payments have been executed. One drug has since failed to demonstrate an effect.
6. **Internal Radiation Therapy Approaches are Validated in Other Cancers, and their Acceptance is Growing** – Sirtex Medical (ASX:SRX; Outperform) utilises a Selective Internal Radiation Therapy (SIRT) approach called SIR-Spheres® in the liver, which has shown to increase survival in patients who have failed prior chemotherapy. They are currently exploring efficacy as a first line treatment in both primary and secondary (metastatic) liver cancer.
7. **Several Pilot Studies Highlighted Potential Benefit** – a 57% improvement in median overall survival was recorded for **OncoSil™** + gemcitabine when compared to the historic data for gemcitabine alone. A disease control rate of 82.4%, with an average reduction in pain of 35% and a maximum of 69% between weeks 8-11 post administration also highlighting promise.
8. **A Single Pivotal Trial may be Sufficient to Deliver an FDA Approval** – as a radiation emitting implanted medical device, **OncoSil™** is likely to be classified as a class III medical device, which will require a Pre Market Approval (PMA) with the FDA and a trial that shows the device is safe and effective for the intended use.

## Valuation

We value **OSL** on a weighted risk-adjusted discounted cash flow basis (rDCF), and discounted P/E and EV/EBITDA basis on FY19 estimates at **\$0.26** per share fully diluted, which forms the basis of our 12 month price target. At this juncture, we believe the licensing of the program upon completion of the pivotal study(s) is more likely or an acquisition of the **OncoSil™** asset.

## OncoSil™ Market Model FY19-FY28

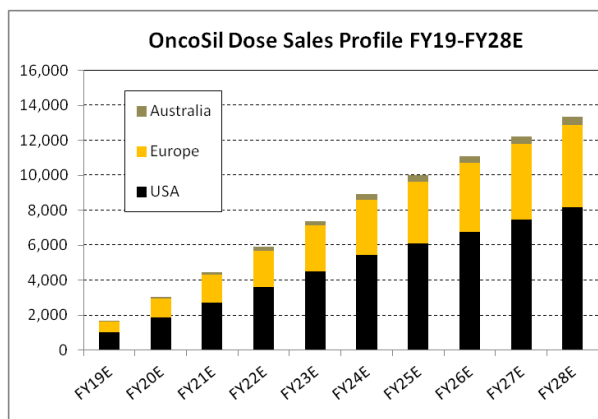
Our market model for **OncoSil™** in locally advanced pancreatic cancer (LAPC) is shown in Appendix 1. We are anticipating that **OncoSil™** will complete and achieve its regulatory filings (US Pre-Market Approval – PMA and CE Mark) by FY19.

The key assumptions underpinning our model are shown below.

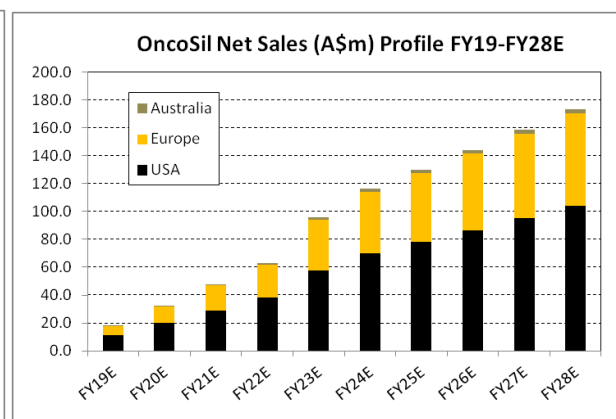
**Assumptions - Revenue Model**

Long term growth rate in incidence	1.2%		
Average Selling Price Year 1-5 (US\$/EUR/AUD'000)	10.0	8.0	6.0
Average Selling Price Year 6-12 (US\$/EUR/AUD'000)	12.0	10.0	7.0
Market share gains (p.a) Year 1-5	3%		
Market Share Gains (p.a) Year 6-11	2%		
Average # Treatments Per Patient	1.5		
Risk-adjustment (chance of success)	66%		

Our doses sold (dose sales) and Net Sales estimates in A\$ terms for **OncoSil™** are shown below.



Source: Taylor Collision estimates



Source: Taylor Collision estimates

**Risk-Adjusted Discounted Cash Flow Analysis (rDCF)**

**OncoSil - WACC Calculation Inputs**

Risk-free rate	3.5%
Market Risk Premium	7.0%
Market Beta	2.00
Cost of Equity	17.5%
Cost of Debt	0.0%
After Tax Cost of Debt (30% TR)	0.0%
D/D+E	0.0%
E/D+E	100.0%
<b>WACC</b>	<b>17.5%</b>

Our rDCF model is shown below. Our rDCF is **\$0.19** (fully diluted)

DCF Valuation

	FY14	FY15	FY16	FY17	FY18	FY19	FY20	FY21	FY22	FY23	FY24	FY25	FY26	FY27	FY28
EBITDA	(1,732)	(2,729)	(6,987)	21,037	18,223	11,476	15,064	18,851	22,775	23,443	28,500	32,098	35,816	39,660	43,633
Change in WC	786	815	1,201	(1,056)	(469)	(1,317)	1,014	212	220	(54)	282	206	214	223	232
Other Non-Cash Items	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500
Tax	0	0	0	0	(2,895)	(1,964)	(2,551)	(3,193)	(3,868)	(4,070)	(9,693)	(10,952)	(12,269)	(13,649)	(15,094)
Capex	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)
<b>Free CFs</b>	<b>(546)</b>	<b>(1,514)</b>	<b>(5,387)</b>	<b>20,381</b>	<b>15,259</b>	<b>8,595</b>	<b>13,927</b>	<b>16,270</b>	<b>19,527</b>	<b>19,719</b>	<b>19,489</b>	<b>21,752</b>	<b>24,161</b>	<b>26,634</b>	<b>29,171</b>
PV of CFs	(546)	(1,514)	(4,584)	14,762	9,406	4,509	6,218	6,182	6,315	5,427	4,565	4,336	4,099	3,846	3,585
<b>Risk Adjustment</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>	<b>66%</b>
Risk Adjusted PV of CFs	(546)	(1,514)	(4,584)	14,762	6,208	2,976	4,104	4,080	4,168	3,582	3,013	2,862	2,706	2,538	2,366
Terminal Value	207,215														
PV Terminal Value	16,806														
<b>% of Enterprise Value</b>	<b>26%</b>														
Enterprise Value	63,527														
Less Net Debt (Cash)	(11,301)														
Equity Value	74,828														
<b>Equity Value Per Share (fully dil.)</b>	<b>\$0.19</b>														

Source: Taylor Collision estimates

We have undertaken the sensitivity of cash flows on a risk-adjusted and no risk basis, which assumes the clinical trial shows an effect, which provides a 37% increase in the DCF value, as shown below.

## Sensitivity Analysis - Enterprise Value (\$'000) (unrisked)

		Terminal Growth Rate				
		2.0%	2.5%	3.0%	3.5%	4.0%
W A C C	15.5%	108,755	110,230	111,822	113,547	115,422
	16.5%	98,767	99,916	101,151	102,480	103,916
	17.5%	90,197	91,103	92,071	93,109	94,223
	18.5%	82,778	83,498	84,265	85,083	85,958
	19.5%	76,302	76,880	77,493	78,145	78,838

Source: Taylor Collison estimates

## Sensitivity Analysis - Equity Value (Unrisked)

		Terminal Growth Rate				
		2.0%	2.5%	3.0%	3.5%	4.0%
W A C C	15.5%	\$0.31	\$0.31	\$0.31	\$0.32	\$0.32
	16.5%	\$0.28	\$0.28	\$0.29	\$0.29	\$0.29
	17.5%	\$0.26	\$0.26	\$0.26	\$0.27	\$0.27
	18.5%	\$0.24	\$0.24	\$0.24	\$0.24	\$0.25
	19.5%	\$0.22	\$0.22	\$0.23	\$0.23	\$0.23

Source: Taylor Collison estimates

## Sensitivity Analysis - Enterprise Value (\$'000) (Risk-adjusted)

		Terminal Growth Rate				
		2.0%	2.5%	3.0%	3.5%	4.0%
W A C C	15.5%	67,910	68,508	69,147	69,832	70,567
	16.5%	64,989	65,587	66,226	66,911	67,647
	17.5%	62,290	62,888	63,527	64,212	64,947
	18.5%	59,791	60,389	61,028	61,713	62,448
	19.5%	57,475	58,073	58,712	59,397	60,132

Source: Taylor Collison estimates

## Sensitivity Analysis - Equity Value (Risk-adjusted)

		Terminal Growth Rate				
		\$0.19	2.0%	2.5%	3.0%	3.5%
W A C C	15.5%	\$0.20	\$0.20	\$0.20	\$0.21	\$0.21
	16.5%	\$0.19	\$0.20	\$0.20	\$0.20	\$0.20
	17.5%	\$0.19	\$0.19	\$0.19	\$0.19	\$0.19
	18.5%	\$0.18	\$0.18	\$0.18	\$0.19	\$0.19
	19.5%	\$0.17	\$0.18	\$0.18	\$0.18	\$0.18

Source: Taylor Collison estimates

Our blended approach, assumes an equally weighted contribution from the rDCF and utilising discounted P/E and discounted EV/EBITDA in the first full year of US and EU sales (FY19), as shown below. The blended methodology provides an equity calculation of **\$0.26** per share, fully diluted which forms the basis of our 12 month price target.

## OSL - Blended Valuation Summary

	Multiple	Weight (%)	Valuation	Blended
rDCF (WACC 17.5%)	n/a	33.3%	\$0.19	\$0.07
Disc. P/E Valuation	20x FY19	33.3%	\$0.34	\$0.11
Disc. EV/EBITDA Valuation	15x FY19	33.3%	\$0.24	\$0.08
<b>Blended Equity Valuation</b>				<b>\$0.26</b>

Source: Taylor Collison estimates

## Comparables

A list of comparable companies to **OncoSil™** is shown below. The most obvious comparable to **OncoSil™** is Sirtex Medical (ASX:SRX, Outperform), which sells a radioactively labelled microsphere ("SIR-Spheres<sup>®</sup>") targeting inoperable liver cancer (primary and secondary). Sirtex has seen a considerable increase in demand for SIR-Spheres<sup>®</sup> as the clinical evidence of effect grows and reimbursement becomes more widespread. In many ways, **OncoSil™** has modelled its business on the success of Sirtex, and the case for loco-regional (where the treatment is restricted to a region of the body, namely liver for Sirtex and pancreas for **OncoSil™**) approaches. We note in terms of takeover multiples for the three acquired companies outlined below, the EV/sales have a median of 3.6x and a mean of 3.8x.

## Comparable Companies

Name	Market Cap (m)	Focus	Product	Sales (m)	% of group revenues
Sirtex Medical (ASX:SRX)	\$791	Interventional Oncology (liver)	SIR-Spheres (Y-90 isotope)	A\$96.8	100%
BTG (LSE:BTG)	£2,000	Interventional Oncology (Liver)	Therasphere, DC-bead*	£28.8	15.4%
		Brachytherapy (prostate)	various	£7.3	
MDS Nordion (TSX:NDN)	US\$648	Interventional Oncology (Liver)	Sold Therasphere to BTG in 2Q CY13 for US\$200m(3.6x sales, 30x EBIT)	US\$56	23%
Biocompatibles (LSE:BGC) * delisted	£177	Interventional Oncology (Liver)	Sold to BTG for £177m (4.9x sales, 42.6x EPS)	£36 (2010)	100%
Nucletron (Elekta)	n/a (Private)	Brachytherapy (various), External Beam	Acquired by Elekta in 2011 for E365m (2.9x sales, 14x EBITDA)	€ 128	100%
IsoRay Medical (NYSE:ISR)	US\$27.6	Brachytherapy	Various - (CS131 isotope)	US\$4.5	100%
OncoSil Medical (ASX:OSL)	A\$48.5	Interventional Oncology (Pancreas)	OncoSil (P-32 isotope)	n/a	n/a

Source: Company reports, Taylor Collison

## Overview on OncoSil Medical and the Pancreatic Cancer Market

**OncoSil Medical** was formed by the acquisition of Enigma Therapeutics (UK) by Neurodiscovery (ASX:NDL) for 75m NDL shares, representing an acquisition value of \$2.85m. Enigma held the w/w license rights to BrachySil (now **OncoSil™**) from pSiMedica, which itself is a subsidiary of pSivida Corporation (ASX: PVA, not rated). A summary of the key terms of the agreement is shown across.

**OSL** has raised \$11.5m in additional equity capital to fund the **OncoSil™** technology into larger randomised controlled clinical studies in locally advanced pancreatic cancer. The Company anticipates launching a major clinical study in the 1H CY14. Prior to the back door listing into ASX:NDL, **OncoSil™** has had approximately US\$25m invested into its development, including two pilot trials, which showed some promise.

Key Terms of The Enigma Acquisition and pSiMedica

Metric	Obligation
Initial Consideration	\$2.55m (75m shares in OSL @3.4c) + US\$100k cash
Annual Fee to pSiMedica	US\$100,000
Royalty on OSL direct Net Sales	8%
Royalty on Any Third Party Payments received (upfront/milestones/net sales)	20%
Milestones	between US\$1m-US\$5m total

Source: OncoSil Annual Report

Pancreatic cancer has one of the worst one and five year survival rates of any cancer. The cancer is normally diagnosed at a late stage which makes surgical options limited, metastatic spread likely, and patients are typically given palliation treatments such as chemotherapy and radiation to extend survival. There have been only two approved chemotherapy treatments for pancreatic cancer that have been shown to extend survival sufficiently to be considered standard of care over the last 16 years.

With the advent of modern minimally invasive surgical options and greatly enhanced guidance systems (i.e. point of care imaging), loco-regional approaches are gaining acceptance medically. In the case of pancreatic cancer, loco-regional approaches for chemotherapy have been utilised historically, but we note no current treatments exist for localised internal radiation therapy, such as **OncoSil™**.

The overall global incidence of pancreatic cancer is approximately 280,000 cases per annum comprising up to 192,000 in developed medical markets such as the US, Europe, Japan and Australia. Given the median overall survival is typically <1 year, the incidence reflects the prevalence of disease in the community. Pancreatic cancer incidence growth has averaged 1.2% p.a over the last ten years.

### What is OncoSil™ Therapy?

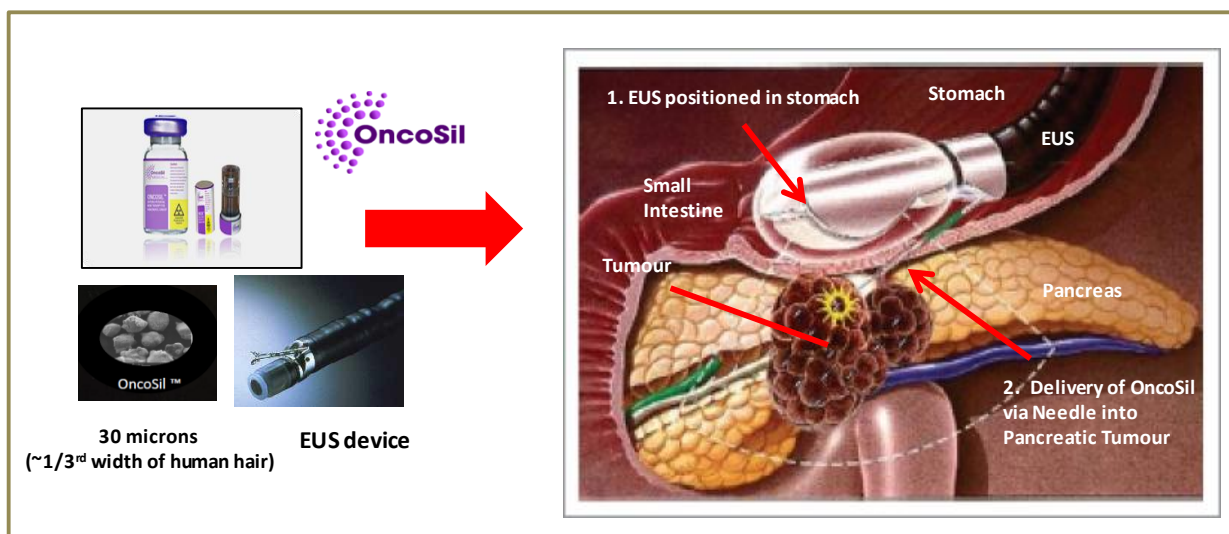
**OncoSil™** therapy is a form of brachytherapy, which is also called internal radiotherapy. By definition it is the delivery of a radiation source placed inside or next to the area requiring treatment. In **OncoSil's** case, the product is delivered into pancreatic tumours (intratumourally). Though brachytherapy is a well established technique in breast and prostate cancer following surgery, it has not garnered widespread use in pancreatic cancer owing to the lack of available imaging technologies to guide deliver of the therapy into the tumours, but also the majority of patients are not eligible for surgery. Unresectable brachytherapy approaches using  $I^{125}$  administered via laparotomy (incision into abdominal cavity) or percutaneously have shown some promise in small clinical studies, but to date there has been no randomised controlled studies in this regard. The major disadvantage of using seeds v **OncoSil™** is the distribution of radioactivity throughout the tumour is significantly easier with **OncoSil™** (as a slurry v a metal seed), and there are mechanical issues on implanting seeds v **OncoSil™** therapy.

Modern therapeutic endoscopic ultrasonography (EUS) has provided the requisite imaging precision to allow for high resolution tumour imaging and the delivery of products directly into the tumour, like **OncoSil**, which consists of a radioactive isotope, phosphorus-32 ( $P^{32}$ ) encased in biocompatible silicon resin.  $P^{32}$  has a half-life of 14.3 days.

**OncoSil™** is administered as a single injection into a locally advanced pancreatic tumour using EUS, as shown below. While the patient is under light anaesthesia, the gastroenterologist passes a tube through the gullet and the stomach until it is in the first part of the small intestine, which is next to the pancreas. The gastroenterologist then uses ultrasound to see where the tumour is located, and passes a very fine needle from the gut to the centre of the tumour. A syringe at the top end of the gastroscop (the tube) to inject **OncoSil™** liquid suspension down the tube and into the tumour. From that perspective, **OncoSil™**

is a major improvement over external beam radiation therapy that has to be delivered daily over six weeks to achieve a similar effect.

### Delivery of OncoSil Treatment to Pancreatic Tumours



Source: OncoSil, Taylor Collison, Du et al., J Interv Gastroenterol, 2011

The procedure takes about 30 minutes. Once inside the tumour, the **OncoSil™** constantly emits radiation over a period of up to three months, slowly destroying tumour cells and reducing in most cases the bulk of the tumour. The radiation is local, there is no damage to the rest of the pancreas, or to surrounding tissues. In several pilot studies there was some leakage of radioactivity into urine and faeces, but this was considered acceptable.

### OncoCal™ Next Generation Platform in Development

In 1Q CY14 **OSL** announced a new development program for OncoCal™ – a derivation of **OncoSil™**, which differs by virtue of when injected it precipitates into an insoluble calcium salt within the interstitial fluid and remains in place. In pilot studies of **OncoSil™** for example, there was a small amount of detectable escape of the radioactive isotope post intratumoural delivery into the faeces and urine, which relates to the use of a biosilicon slurry. The phosphorus-32 content on OncoCal™ is higher than **OncoSil™**, potentially providing a COGS advantage and smaller delivery volume and enhanced distribution within the tumour (greater radiation effects). The **Company** has filed patents on the new application, which if granted will provide coverage until 2032 (without extensions).

### Pricing

The US\$ cost of Abraxane® in pancreatic cancer is US\$6,000-US\$8,000 per month, inferring a total cost per patient of US\$51,000-US\$68,000 for 8.5 mths of overall survival (1.8 month benefit over gemcitabine). We have taken a more conservative view on **OncoSil™** pricing than management, and believe a US list price of US\$10,000 with an average of 1.5 treatments per patient is appropriate. The **Company** believes it can sell **OncoSil™** for US\$15,000 per dose (identical to ASP of Sirtex's SIR-Spheres®), but given the expected benefit for **OncoSil™** v that of SIR-Spheres® will likely be narrower (pilot study ~4.8 mth OS benefit v majority of SIR-Spheres® data at +6 mths), there is a case for a lower ASP for **OncoSil™**, unless the clinical trials demonstrate a very significant OS benefit above the 3 months we believe is sufficient to garner clinical adoption.

We note some analysis from the National Institute of Health and Care Excellence (NICE) in the UK which showed total treatment cost per patient on Gemzar® (gemcitabine) was estimated at £3,569 and on 5-FU at £1,262 — the incremental cost-per-life-year-gained on Gemzar® was £12,206 and the incremental cost-per-progression-free-life-year gained was £19,888.

### OncoSil™ will be Regulated as a Class III Medical Device

The US FDA classifies implantable radioactive medical devices as Significant Risk (SR) devices. An SR device presents a potential for serious risk to the health, safety, or welfare of a subject. SR devices may include implants, devices that support or sustain human life, and devices that are substantially important in

diagnosing, curing, mitigating or treating disease or in preventing impairment to human health. As a result, the upcoming study of **OncoSil™** will require an Investigation Device Exemption (IDE) to conduct a US trial. **OncoSil™** has indicated it will file an IDE in the near term.

From our discussion with the FDA, it would consider an implantable radioactive device as a Class III device that requires premarket approval (PMA). This designation has been confirmed by **OSL**. The FDA defines a Premarket Approval (PMA) application as “a scientific, regulatory documentation to FDA to demonstrate the safety and effectiveness of the class III device.” For context, both SIR-Spheres® and Therasphere® Y-90 radiation devices for liver cancer are regulated in this manner.

We note in recent FDA industry guidance (November, 2013) for PMA's: *The FDA through regulation, interpreted the statutory standard for approval of a PMA as follows:*

21 CFR 860.7(d)(1). *There is reasonable assurance that a device is **safe** when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use.*

21 CFR 860.7(e)(1). *There is reasonable assurance that a device is **effective** when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.*

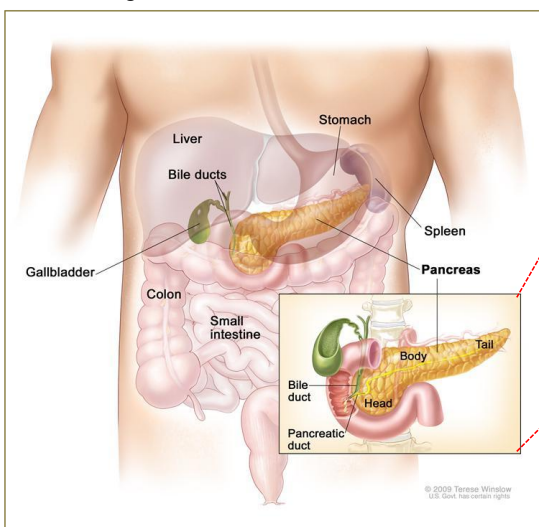
Therefore, as a class III regulated device undertaking a PMA process, we believe **OncoSil** will need to show effectiveness in a statistical manner on the primary endpoint (i.e. overall survival) of major trials planned, to be considered for approval under a PMA.

## What is Pancreatic Cancer?

Primary tumours of the pancreas are divided into adenocarcinoma (95% of cases) which is a cancer of the exocrine cells of the pancreas which produces gastric juices and neuroendocrine (NET) tumours (5%) which is a cancer of the endocrine or hormone producing cells of the pancreas (e.g. islet cells that produce insulin). **OncoSil™** therapy will be targeting adenocarcinoma patients. From the perspective of surgical options for pancreatic cancer, there are cancers emanating in the head, body and tail, as shown below. Approximately 80% of all cancers arise in the head, 15% in the body and 5% in the tail.

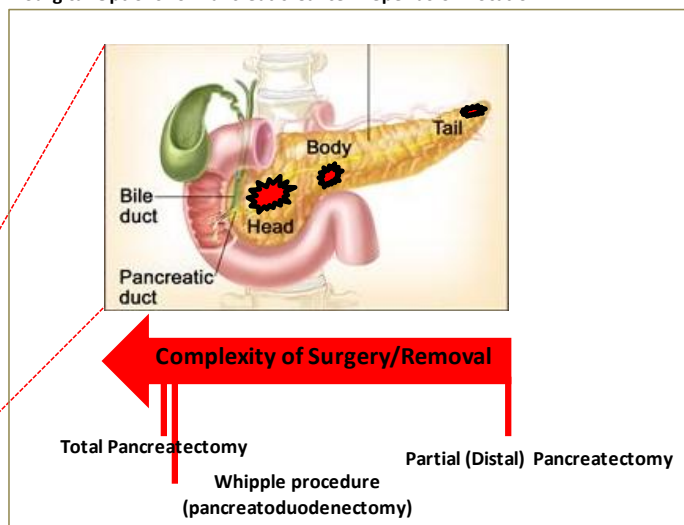
Approximately 15% of pancreatic cancer patients have disease which is amenable to surgical interventions. Surgical success for the most part depends on the location of the primary tumour within the pancreas – which is divided into the head, body and tail, as shown below right.

Understanding the Pancreas



Source: National Cancer Institute

Surgical Options for Pancreatic Cancer Depends on Location



Source: National Cancer Institute, Taylor Collison

The problem with a tumour in the tail and to a lesser extent the body of the pancreas is that patients are

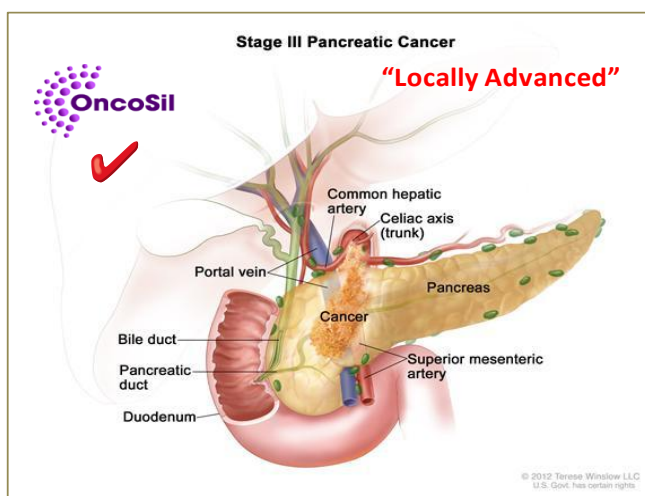


often asymptomatic, thus by the time the tumour is diagnosed, it has already spread locally (locally advanced) or gone metastatic, all of which typically rule out surgical options (partial pancreatectomy). **OncoSil™** is targeting late stage II /stage III and stage IV pancreatic cancer (stage I is where the cancer is localised to the pancreas only). Stage III and stage IV patients are not candidates for surgery.

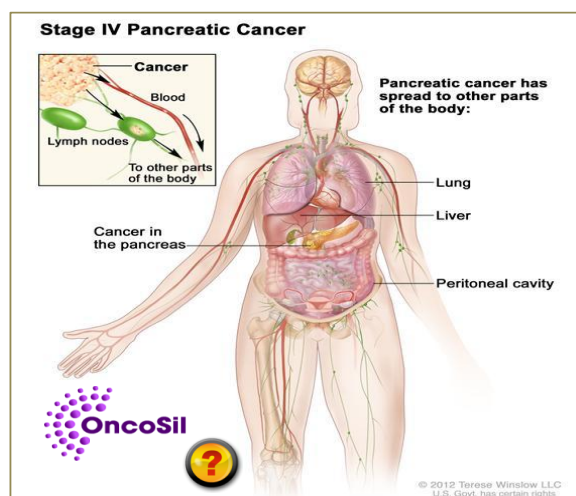
According to the National Cancer Institute (NCI), Stage III pancreatic cancer is defined by the spread to the major blood vessels near the pancreas. These include the superior mesenteric artery, celiac axis, common hepatic artery, and portal vein (see below). Cancer may have spread to nearby lymph nodes. Patients have a 6-10 month survival outlook with median one year survival of 26%.

Stage IV pancreatic cancer is where the cancer has spread to distant organs, such as the lung, liver, and peritoneal cavity (the space in the abdomen that contains the intestines, stomach, and liver). Cancer may also have spread to tissue and organs near the pancreas or to lymph nodes (see below). **OncoSil™** is perfectly suited to stage III disease may be considered for stage IV patients for control of tumours in the pancreas. For patients with stage IV disease the best available standard of care treatments provide for median overall survival of approximately 8.5 months. Patients who refuse or are ineligible for treatment with Stage III/IV disease have a life expectancy of <6 months.

### Stage III (locally advanced) and Stage IV (metastatic) Pancreatic Cancer



Source: National Cancer Institute, Taylor Collison



Source: National Cancer Institute, Taylor Collison

Pain and associated Quality of Life (QOL) are major factors in pancreatic cancer, given the rapid progression of disease and poor <12 month overall survival prognosis. Severe pain is associated with the tumour invading nerves or organs in close proximity to the pancreas, and blockages of the various digestive tracts. For severe pain, a celiac plexus block is performed which aims to destroy the branched abdominal nerves associated with pain signalling. Both chemotherapy and chemoradiotherapy interventions have been shown to improve tumour pain. For locally advanced tumour control, we see **OncoSil™** as potentially beneficial.

### Incidence of Pancreatic Cancer and Survival

The American Society of Clinical Oncology estimates that in the US, pancreatic cancer is the 10<sup>th</sup> most common disease in men and 9<sup>th</sup> most common in women, and the 4<sup>th</sup> leading cause of death. Annual US incidence for CY13 was estimated at 45,220 with 38,460 deaths. In the European Union, the annual incidence is 39,084 cases, with 26,234 out of countries we believe have the necessary reimbursement infrastructure to support sales of **OncoSil™** (and reflective of major markets for Sirtex in Europe), as shown across. In Australia, there were 2,546 new cases recorded in 2009.

The global market for pancreatic cancer drugs is projected to exceed US\$1.2 billion by 2015 according to GIA, Inc. However, Decision Resources anticipate a markedly different market with the current market valued at US\$700m, growing to US\$829m by 2019. The difference probably relates to differences in timing of patent expiration and generic pricing.

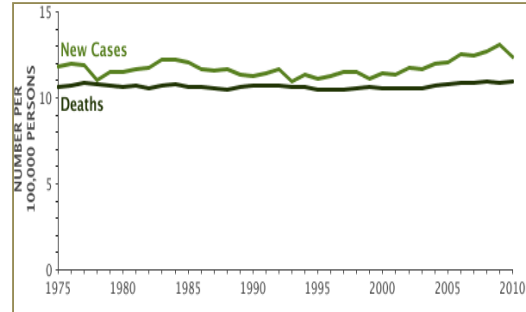
European Incidence of Pancreatic Cancer

Country	Incidence
UK	4,211
France	4,555
Germany	7,972
Italy	4,946
Spain	3,335
Switzerland	548
Belgium	667
<b>EU (7)</b>	<b>26,234</b>
<b>EU (27)</b>	<b>39,084</b>

Source: WHO (EUCAN)

Pancreatic cancer is often difficult to diagnose as there are no screening tests to detect early stage disease (unlike breast, colon cancer for example). As a result, by the time symptoms appear the cancer has already advanced within the pancreas and surrounding tissue and blood vessels (locally advanced) spread to distant organs such as the liver (metastatic disease). As only 10-15% of all newly diagnosed are eligible for surgery to remove the cancer, the disease is for the most part terminal with survival extended only marginally with chemotherapy or radiotherapy regimens. More recent chemotherapy regimens have seen overall survival increases from locally advanced/metastatic forms of the disease from approximately 4 months to 8.5 months.

The one year survival rate is approximately 26% and the five year survival rate is 6%. In the US, since 1975, the five year survival has doubled from 3.0%, though as discussed patients have a very poor outlook following diagnosis. To give context, colon cancer survival is 65% and breast cancer 89% and prostate cancer 100% at five years. The ten year CAGR in the US for incidence shows pancreatic cancer has grown 1.2% p.a since 2000, as shown across.

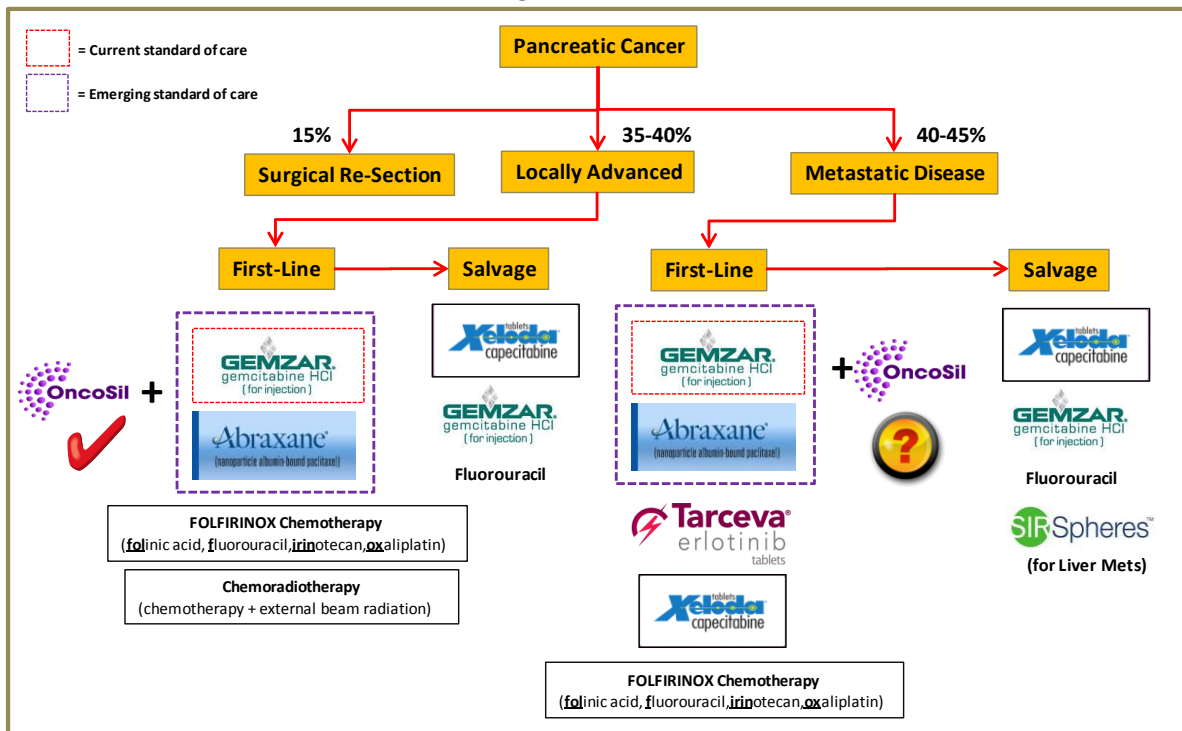


Source: cancer.gov

### Treatment Schema for Locally Advanced/Metastatic Pancreatic Cancer

The treatment schema for adenocarcinoma (95% of all cases) is shown below. Both Xeloda® and Gemzar® are now generic. The schema is based on the National Comprehensive Cancer Network (NCCN) recommendations for locally advanced and metastatic disease. We note the recent inclusion of Abraxane® into these guidelines following a very strong clinical trial result, as discussed later.

#### Pancreatic Cancer Treatment Paradigm



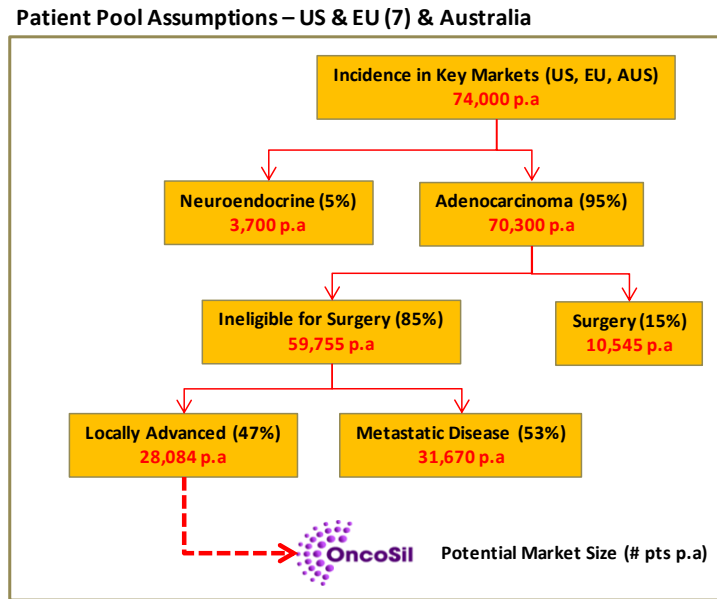
Source: Taylor Collison

We see **OncoSil™** as a viable treatment option in locally advanced disease. For those with metastatic disease, we would consider **OncoSil™** as a viable treatment in those with very limited metastatic disease where local control of tumour burden is required.

### The Market Size for OncoSil™

Based on incidence data for the US and Europe and Australia, and the treatment schema presented above, we have defined the exploitable market opportunity for **OncoSil™** as 28,084 patients per annum,

as shown below. We have excluded Japan as a market for **Oncosil™**, based on the complexity of the regulatory process in Japan for radiopharmaceuticals, and the lack of effect shown in an Asian population by **Oncosil's** intended clinical plan. The intended clinical plan will result in a CE Mark (Europe) or PMA (USA) and TGA approval in due course. Our calculations are shown below.



Source: Taylor Collison estimates

While there is scope for use of **Oncosil™** in metastatic disease to control tumours in the pancreas, it is very unlikely that it will show a benefit in overall survival where metastases are prevalent, given the destination for a high percentage of metastases is the liver, though which patients ultimately succumb to their disease. However, it could conceivably be used to control tumour growth in the pancreas and to help alleviate pain.

As a loco-regional therapy for the pancreas, **Oncosil™** is uniquely suited to control disease in the pancreas, which for locally advanced disease may reduce the likelihood of disease spread and further local invasion, which may be beneficial to survival over standard of care.

## Oncosil™ a Uniquely Placed Treatment Modality for Pancreatic Cancer

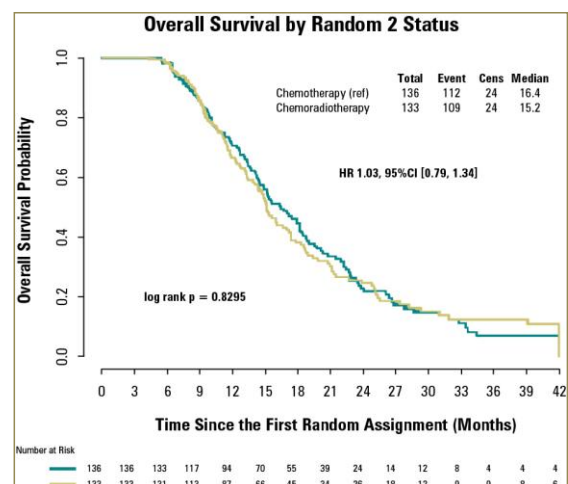
We have identified several reasons why a new treatment approach, such as internal radiation therapy using **Oncosil™** is desirable for pancreatic cancer, as highlighted below.

### Surgery is Only Possible in 10-15% of all new cases

As discussed, the fact there is no screening test for pancreatic cancer means that diagnosis on the basis of patient symptoms means in 85-90% of cases, the cancer is inoperable (unresectable). Current standard of care chemotherapy in locally advanced pancreatic disease seeks to downstage tumour burden to allow for re-section, which provides the strongest likelihood of a cure.

### External Beam Radiation Does Not Improve Overall Survival

Radiation therapy is considered a standard of care in the treatment of locally advanced pancreatic cancer in combination with chemotherapy (chemoradiotherapy). However, recent evidence suggests it does not improve overall survival in patients, when combined with chemotherapy. Despite advances in external beam radiation, a 2013 Phase 3 randomised controlled study showed that for patients with locally advanced pancreatic cancer where the disease was controlled with gemcitabine-based chemotherapy and gemcitabine plus the addition of Tarceva® (erlotinib, more below).



Source: Hammel J. Clin. Oncol, 2013

Patients with controlled disease were then assigned to receive radiation therapy and capecitabine chemotherapy. The results showed that the addition of Tarceva<sup>®</sup> and chemoradiotherapy did not improve overall survival ( $p=0.83$ ) in these patients.

The authors concluded “Erlotinib was not beneficial in locally advanced pancreatic cancer, and increased toxicity, and neither radiation nor erlotinib improved survival. This trial may change practice, and certainly generates many questions for future trials.” Other meta analyses had indicated chemoradiation therapy improved OS and increased downstaging of tumours to allow resection. The data above implies the tumour shrinkage effects may be gemcitabine related only (see more below).

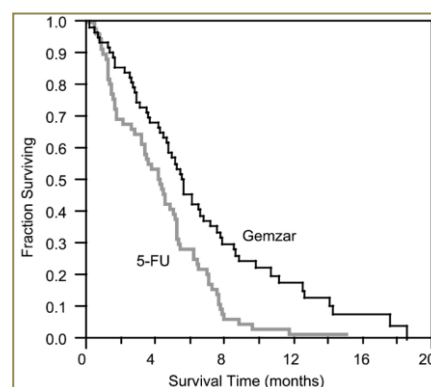
In recognition that all forms of radiation typically kill dividing cells and the nature of pancreatic cancer is such that small doses are given over a number of weeks, rather than a large dose in isolation. A therapy like **Oncosil** which emits radiation within the tumour over a number of weeks continually may be expected to work synergistically with gemcitabine, which is a potent radiosensitiser and impacts on cell replication and cell death.

## New Drugs for Locally Advanced / Metastatic Pancreatic Cancer are Lacking

The two standard of care (SOC) chemotherapy agents for treatment of advanced pancreatic cancer (LAPC and metastatic) are gemcitabine and Abraxane<sup>®</sup>. Other chemotherapy agents including FOLFIRINOX chemotherapy, erlotinib (Tarceva<sup>®</sup>) and fluorouracil are also used, as shown previously/.

### Gemcitabine was approved 18 years ago

In the pivotal registration study ( $n=126$ ), gemcitabine (Gemzar<sup>®</sup>) increased median overall survival from the then SOC 5-fluorouracil of 4.2 months to 5.7 months, or 35.7%, as shown across ( $p=0.004$ ). Interestingly, neither therapy showed any objective response on tumours (no shrinkage under RECIST). The result crystallised an immediate change in treatment regimens such that Gemzar<sup>®</sup> rapidly became the SOC and remains that way today. The drug was approved in 1996. The drug has now gone generic. Given its preferred status as a front-line therapy, which is unlikely to change in the medium term in our view, drug developers need to show a benefit in combination with gemcitabine in OS. To date, this has proved very challenging, until very recently with the data from a randomised Phase 3 trial of Abraxane<sup>®</sup>.



### Abraxane (Nab Paclitaxel) – Emerging Gold Standard in the US and Europe

On September 6, 2013, the FDA approved paclitaxel albumin-stabilized nanoparticle formulation (Abraxane<sup>®</sup>) in combination with gemcitabine for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas. The approval was based on the demonstration of improved overall survival (OS) in a multi-centre international, open-label randomised trial that enrolled 861 patients with metastatic pancreatic cancer. Patients were randomly assigned to receive either paclitaxel albumin-stabilized nanoparticle formulation plus gemcitabine ( $n=431$ ) or gemcitabine alone ( $n=430$ ). The major efficacy outcome measure was OS.

The median OS was 8.5 months in patients treated with paclitaxel albumin-stabilized nanoparticle formulation plus gemcitabine and 6.7 months in patients treated with gemcitabine alone [HR 0.72 (95 percent CI: 0.62, 0.84);  $p < 0.0001$ , stratified log-rank test]. A significant improvement in progression-free survival (PFS) was also observed, with median PFS of 5.5 months in patients treated with paclitaxel albumin-stabilized nanoparticle formulation plus gemcitabine and 3.7 months in patients treated with gemcitabine alone [HR 0.69 (95 percent CI: 0.58, 0.82)  $p < 0.0001$ , stratified log-rank test]. Objective response rates (ORR) were 23 percent in patients treated with paclitaxel albumin-stabilized nanoparticle formulation plus gemcitabine and 7 percent in patients treated with gemcitabine ( $p < 0.0001$ ).

In November, 2013 the European Medicines Agency (EMA) approved Abraxane<sup>®</sup> for metastatic pancreatic cancer based on this study result. The National Comprehensive Cancer Network (NCCN) guidelines (Appendix 1 and Appendix 2) now recommend its use as a first-line therapy.

As a result, the standard in pancreatic cancer (locally advanced and metastatic) is now gemcitabine + Abraxane<sup>®</sup> which means the survival curve for **Oncosil**<sup>™</sup> shifts from a benefit of 6.7 mths to 8.5 months.

## **Tarceva® (Erlotinib) – Menial Benefit, Limited Use**

Tarceva® (erlotinib) was approved by the FDA in 2005. The safety and efficacy were demonstrated in a single, multicentre (U.S. and international), double-blinded, placebo-controlled, randomized, phase 3 study of erlotinib plus gemcitabine versus gemcitabine plus placebo as first-line chemotherapy for locally advanced or metastatic pancreatic carcinoma. The study involved 569 patients.

The primary endpoint of the trial was overall survival. Survival was prolonged on the erlotinib arm with a median overall survival of 6.4 months and 6.0 months in the placebo/gemcitabine groups, respectively. The adjusted Hazard Ratio (HR) for death in the erlotinib group relative to the placebo group was 0.81,  $p = 0.028$ . The drug is not considered an effective treatment in pancreatic cancer based on this data and as a result has not been widely adopted.

## **Other Drugs have Failed to Show an Effect**

Consistent with late diagnosis and poor prognosis generally, chemotherapy agents in the most part have failed to show any benefit in late stage pancreatic cancer.

In late 2012, a pivotal Phase 3 study in 348 patients for masitinib showed the overall study population did not show a significant advantage for masitinib in combination with gemcitabine as compared with gemcitabine treatment alone. Median OS was 7.7 months in the masitinib plus gemcitabine treatment arm versus 7.0 months in the placebo plus gemcitabine treatment arm ( $p=0.74$ ; hazard ratio=0.90).

Another drug, which is discussed below in more detail, called regosertib was very recently pulled (late 4Q CY13), after an interim analysis showed it did not confer a survival advantage over gemcitabine alone.

## **Pain Reduction a Potential Side Benefit of OncoSil™**

While there is no standard of care in the management of pain in pancreatic cancer, anti-inflammatory agents, opioids, radiation therapy, chemotherapy, and celiac plexus neurolysis (CPN) are used widely. OncoSil™ showed an average reduction in pain of 35% and a maximum of 69% between weeks 8-11 post administration in pilot studies conducted to date (see below).

CPN has a long-lasting benefit in patients with pancreatic cancer. A meta analysis showed a complete or partial pain reduction in 90% of patients to 3 months and 70-90% until death. CPN is safe, with common mild side effects and uncommon severe adverse effects. It is an alternative to opioid analgesics, both for improving pain control and for avoiding or reducing the side effects of high-dose opioids, which can significantly hinder QOL. While **OncoSil™** showed improvement in pain scores in pilot studies, it was also able to increase PFS and OS versus historic controls, a key differentiator to CPN (see below).

It is accepted that CPN does not prolong survival in pancreatic patients. However, Endoscopic Ultrasound (EUS) guided CPN is becoming more common, given the overall improved real-time visualisation and reduced risk of major (neurologic) complications. It is also a significantly cheaper intervention for pain control than **OncoSil™** would represent (if outcome is pain only).

## **Neoadjuvant Use Could Materially Improve Re-Section rates in LAPC**

The administration of **OncoSil™** to down-stage previously unresectable LAPC to being surgically resectable is an important consideration of its likely benefits in our view, and clinically very meaningful. We note a recent study (2012 Hosein *et al.*, BMC Cancer), which examined the combination of Gemcitabine + FOLFIRINOX chemotherapy in unresectable LAPC patients. Though a small sample size of 16 pts, the study showed an R0 (where all the cancer is removed and clear normal margins exist) resection rate of 44%. Such benefits for **OncoSil™** treatments remain a critical feature for this intervention.

## **Pilot Trials for OncoSil Showed Promise**

**OncoSil™** has completed two small pilot programs in pancreatic cancer, both of which showed some evidence of effect.

### **First Pilot Study**

The design of this initial study was a single intra-tumoral injection of 100 Gy (Gray Unit, a measure of radiation) of **OncoSil™** following gemcitabine administration or within three days post in 17 patients (1

patient withdrew). The key efficacy results were an overall disease control rate of 82.4%, with an average reduction in pain of 35% and a maximum of 69% between weeks 8-11 post.

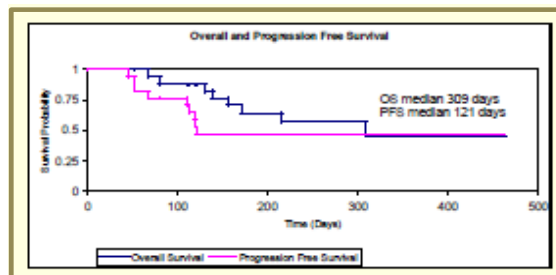
Median overall survival was an impressive 309 days (10.16 mths) and progression free survival (PFS) of 121 days, as shown below. For context, gemcitabine OS is ~6 months and PFS 3.7 months. Of the 17 patients recruited, six had locally advanced disease, 11 metastatic disease. 76% of patients exhibited good performance status when enrolled. The results should be viewed with caution, as the sample size is small and the nature and extent of distant metastases, unknown. As discussed, we would not expect **OncoSil** to impact survival significantly in those patients with metastatic disease outside of pancreas.

Efficacy Results - Pilot

Response	No.	%
CR	0	0
PR	2	11.8
SD	12	70.6
PD	2	11.8
Withdrawn	1	5.9

CR- complete response; PR – partial response; SD – stable disease; PD – progressive disease  
 Source: Ross et al, ASCO presentation; Modified by Taylor Collison

Survival Curves



Source: Ross et al, ASCO presentation; Modified by Taylor Collison

No clinically significant adverse events related to **OncoSil™** were apparent. The procedure time in this study was 5-12 minutes, with 3-6ml of **OncoSil™** injected into the tumour. The excretion of the radioisotope was also examined, with 6/17 patients having detectable radioactivity in the urine, though excretion appeared to be via faeces. The levels were considered small enough to not pose any threat to environmental health.

## Second Pilot Study

The second study on six patients was originally designed as a dose escalation study (200 to 400 Gy – Gray Units) in six patients monitored until death in combination with gemcitabine chemotherapy. 100% of the patients showed disease stabilisation as shown below, over the 24 week study period. The trial was discontinued thereafter, however no deaths on study were noted following 24 week follow up of the last patient. Of the adverse events, none were definitively linked to administration of **OncoSil™**.

Target Tumour Response Rate (ITT population)			
Absorbed dose of 32P BioSilicon (BrachySil™) <b>Now OncoSil</b>	200 Gy	400 Gy	Overall
	N=3	N=3	N=6
Target tumour response (PR or CR)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Target tumour control rate (PR or CR or SD)	3 (100.0%)	3 (100.0%)	6 (100.0%)
- CR	0	0	0
- PR	0	0	0
- PD	0	0	0
- SD	3 (100.0%)	3 (100.0%)	6 (100.0%)

PR, partial response; CR, complete response; SD, stable disease; PD, progressive disease.

Source: OncoSil

## Pivotal Study Design Considerations

**OncoSil™** has proposed a trial design which will recruit up to 150 patients (400 Gy dose) with LAPC and good overall performance status. An interim analysis on 30 patients, examining the surrogate for OS, namely Progression-free survival (PFS) will be undertaken for futility (see below).

The 2:1 randomisation will be gemcitabine +/- Abraxane® + **OncoSil™** versus gemcitabine +/- Abraxane® alone. Based on the recent shift in Standard of Care (SOC) we believe most patients in the two arms will receive gemcitabine and Abraxane®.

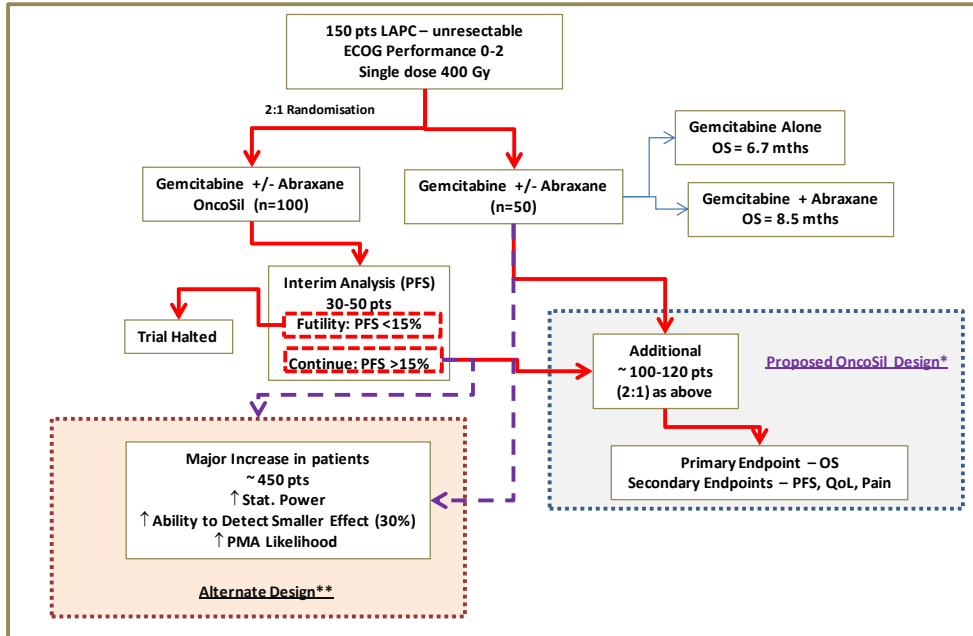
We believe the current proposed trial of 150 patients randomised 2:1 is designed to improve overall survival by ~53% which equates to an additional **4.5 months** over SOC now at **8.5 months** (per Abraxane® registration study), for a total OS in the **OncoSil™** arm of **13 months**. This is an aggressive trial design relative to the hurdle required for acceptance of 30% improvement in our view. The envisaged current trial has been designated a PMA “support” study. In other words, the trial will not deliver a statistically significant result if **OncoSil™** fails to replicate the benefit (in months) over SOC in pilot study results.

We consider this a reasonable possibility, given single-arm studies like the pilot study are subject to bias, there has been a SOC change since the trial and importantly, gemcitabine alone delivered 6.5 months median OS in the most recent Abraxane® registration study in pancreatic cancer patients (up from 5.7 months when gemcitabine was approved 18 years ago).

From our discussions with an industry contact, a clinical trial with 80% power to detect a 2.6 month benefit

of **OncoSil™** over Abraxane® and gemcitabine alone (i.e. 11.1 mths from 8.5 mths, or 30% improvement), could require a total sample size of up to 600 patients, which is highlighted below. The Company has incorporated an adaptive element into its design via the interim analysis based on PFS in 30 patients on trial for six months. We advocate an expanded trial following the interim analysis, as shown below. This will require further funding but if the result is strong enough, it is worth adapting the study to ensure success at a lower OS threshold in our view.

**OncoSil Clinical Trial Schema “PMA Support Study”**



\* Per Investor Presentation Dec 2014, Investor Newsletter Jan 2014. \*\* Taylor Collison est. OS – overall survival; PFS – progression free survival; QoL – quality of life  
Source: Company reports, Taylor Collison

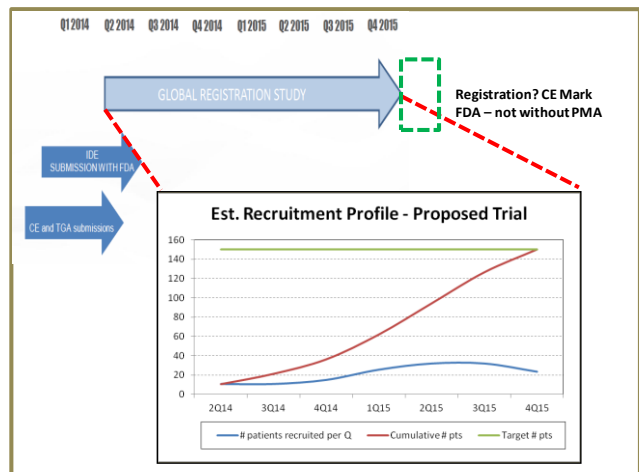
If **OncoSil™** delivers a statistically significant result on the 150 patient study, there is no doubt in our mind the FDA will approve the treatment, as it would have delivered one of the strongest percentage increases in overall survival ever seen in an oncology trial. However, this is very unlikely as a pancreas only treatment (the patients could also succumb to metastatic disease, which **OncoSil™** does not target). Therefore, at best the treatment will slow metastatic spread and local invasion and conceivably increase OS. From our discussions, any result >30% benefit in LAPC is considered clinically meaningful.

If **OncoSil™** delivers a 30% result on the current envisaged design, it will be a non-significant study, but confer a trend. Consequently, it is highly likely the results will not be accepted by the FDA under a PMA (misses the “effectiveness” requirement –  $p < 0.05$ ). In general, larger differences between groups are easier to uncover than small differences, but paradoxically a small benefit is all that is required in LAPC to be considered a SOC. It is therefore wise to power a study to detect a smaller benefit to insure against the prospect the results are non-significant if a higher than required benefit is sought. As discussed, **OncoSil™** need only show a 30% benefit to garner sizeable clinician interest.

The original design plan suggests a 12 month recruitment period, with an additional 12-18 month follow up period for measuring overall survival. Twenty centres will be involved in the study – 6 in Australia, 1 in Singapore, 3 in the US and 10 in Europe. The recruitment profile and our estimates of the recruitment rate is highlighted across.

While the study may be sufficient to secure a CE Mark in Europe (if one is not forthcoming based on pilot studies – see below), if designated as a class III device in the US (highly likely) then the PMA pathway is required. As discussed, we do not envisage an approval for **OncoSil™** in the US if the current trial delivers a non-significant result with the 150 patients targeted for recruitment.

**Clinical Trial Recruitment Profile**



Source: OncoSil, Taylor Collison estimates

## Manufacturing

**OSL** manufacturing involves a five step process, as shown across. The advantage of biosilicon unlike other materials is its chemical properties as a carrier for  $P^{32}$  are not altered during the radiation process to create the  $P^{32}$  from phosphorus. A single powered vial is shipped to users for reconstitution in a proprietary formulation developed by OSL, prior to delivery into the patient.

From our perspective, the rate limiting step is continued manufacturing access to a high neutron reactor for the creation of radioactive particles. Owing to the need for a reactor versus a mixing chamber (such is the case for Sirtex SIR-Spheres<sup>®</sup>)

**OSL** will always require third party manufacturing expertise.

The half life of  $P^{32}$  (14.3 days) permits some greater flexibility in the logistics required to deliver the product to treating hospitals versus other radioactive isotopes (Y-90 in SIR-Spheres<sup>®</sup> has a half life of 64 hours). As such there would be efficiencies in the manufacture process in our view. OncoSil<sup>™</sup> anticipate margins in excess of 85% for the product.

In July 2013 **OSL** announced a cooperation and costs sharing agreement with Eckert & Ziegler, a leader in the manufacture of devices, radiochemicals and radiopharmaceutical precursors used in the treatment of serious diseases and for medical imaging. Eckert had 2012 sales of €120 million. The companies intend to enter into a formal process development and manufacturing agreement over time.

The **Company's** intention is for the final agreement to permit manufacture of **OncoSil's** radiochemical device, **OncoSil<sup>™</sup>**, to be conducted in the Good Manufacturing Practice (cGMP) compliant facilities in Germany. It is also intended to utilise Eckert & Ziegler's expertise in global shipping of radioactive packages.

## CE Mark for OncoSil?

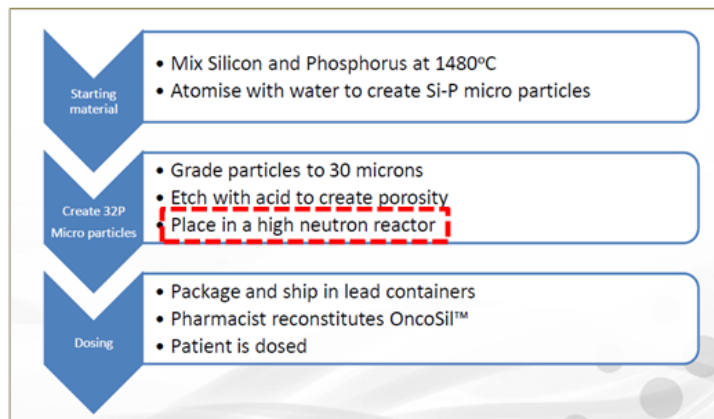
Generally, a CE Mark does confirm the safety of a device, but it does not confirm its effectiveness – this is a key differential to the US FDA. If **OncoSil<sup>™</sup>** is regulated as a class III medical device, it will require clinical data for CE Mark (see Appendix 4). In that respect, will a major trial be required, beyond the initial pilot trial? Time will tell. The Company anticipates making investigations into a CE Mark on an ongoing basis. It is therefore possible, based on the EU directive below that OSL has satisfied the requirements for a CE mark based on its trial result.

We note the EU council directive 93/42/EEC, that *"in the case of implantable devices and devices in Class III clinical investigations shall be performed unless it is duly justified to rely on existing clinical data. The clinical evaluation and its outcome shall be documented. This documentation shall be included and/or fully referenced in the technical documentation of the device."*

Some brachytherapy devices, which do not emit the same level of radiation as **OncoSil<sup>™</sup>** are classified as Class IIa or Class IIb, which has less onerous clinical requirements and do not necessarily require clinical data. However, we understand the classification **OncoSil<sup>™</sup>** will be class III.

We note the CE Mark, as the less onerous and less costly option will deliver **OncoSil<sup>™</sup>** an approval for the intended indication (LAPC), but will not guarantee sales and reimbursement without a clear demonstration of improvement in overall survival (OS). However, such a strategy will ensure the a number of early stage adopters can gain experience with its use outside of the proposed clinical trial.

### OncoSil<sup>™</sup> Manufacturing Process



Source: OncoSil Medical, Taylor Collison



## Pharmaceutical Company Interest in Pancreatic Cancer is Intense

Reflecting the unmet medical need in pancreatic cancer, we have identified two very significant license deals in pancreatic cancer over the last 18 months that collectively were worth over US\$1 billion in biodollars.

In 1Q CY13, Threshold Pharmaceuticals (NASDAQ:THLD), market cap US\$300m, licensed TH-302 to Merck KGaA in a deal worth US\$550m in upfront (US\$25m) and milestone payments and the assumption of 70% of the development costs. Total potential milestone payments are US\$525 million, comprised of US\$280 million in regulatory and development milestones and US\$245 million in sales-based milestones. The main programs are in pancreatic cancer and soft tissue sarcoma.

TH-302 is a hypoxia-targeted drug that is thought to be activated under tumor hypoxic conditions, a hallmark of many cancer indications. Areas of low oxygen levels (hypoxia) within tissues are common in many solid tumors due to insufficient blood vessel growth.

The MAESTRO study was commenced in early 2013 and is a multi-centre, double blind placebo controlled study of TH-302 + gemcitabine v gemcitabine alone in 660 unresectable locally advanced or metastatic pancreatic cancer patients. The study has gained Special Protocol Assessment (SPA) status from the FDA. The Phase 3 MAESTRO study for TH-302 was initiated following results from a randomized, controlled Phase 2b trial of TH-302 in patients with pancreatic cancer.

At the ESMO 2012 Congress (European Society for Medical Oncology) updated Phase 2 b results (n=214) were presented confirming a significant improvement (p=0.008) in PFS associated with 41% reduction of risk for disease progression or death for patients treated with TH-302. This represented a 2.4-month increase in median PFS, while the 12-month overall survival rates were also in favour of the TH-302 340 group compared with the control arm (38% vs 26% (p=0.13)).

In 3Q CY12, Onconova Therapeutics, Inc. (NASDAQ:ONTX), market cap US\$290m, announced a European license deal for Regosertib with Bayer in a deal worth up to US\$565m, including US\$50m upfront. Regosertib's mechanism of action targets dual pathways (PI-3K and PLK) critical to the growth of cancer cells. At the time of licensing the company was conducting a Phase 3 trial in pancreatic cancer and Myelodysplastic Syndromes (MDS).

A multi-centre Phase 3 program comparing regosertib sodium in combination with gemcitabine v gemcitabine alone completed recruitment (n=650) and was expected to report in late 2014. However, in late 2013 the developers Onconova discontinued its Phase 3 study based on an interim analysis showing it was unlikely to show a statistically sig. improvement in OS.

## Patent Position

A summary of the issued and pending patents is shown below. Essentially post acquisition, **OSL** is the registered owner of the two patent families covering **OncoSil™**

The Core US patent expires in 2022, with the potential for patent extensions to 2027. A summary of key patent jurisdictions, shown below.

Official No.	Owner	Title	Country	Application Date	Registration Date	Status
4594587	pSiMedica Limited	Devices and methods for the treatment of cancer	Japan	20-Feb-2002	24-Sep-2010	Granted
5280188	pSiMedica Limited	Devices and methods for the treatment of cancer	Japan	20-Feb-2002	31-May-2013	Granted
8097236	pSiMedica Limited	Devices and methods for the treatment of cancer	USA	20-Feb-2002	17-Jan-2012	Granted
8647603	Enigma Therapeutics Limited	Devices and methods for the treatment of cancer	USA	20-Feb-2002	11-Feb-2014	Granted
1361899	pSiMedica Limited	Devices and methods for the treatment of cancer	France	20-Feb-2002	22-Nov-2006	Granted
60216234.3	pSiMedica Limited	Devices and methods for the treatment of cancer	Germany	20-Feb-2002	22-Nov-2006	Granted
1361899	pSiMedica Limited	Devices and methods for the treatment of cancer	Spain	20-Feb-2002	22-Nov-2006	Granted
1361899	pSiMedica Limited	Devices and methods for the treatment of cancer	Italy	20-Feb-2002	22-Nov-2006	Granted
1361899	pSiMedica Limited	Devices and methods for the treatment of cancer	United Kingdom	20-Feb-2002	22-Nov-2006	Granted
06020790.9	pSiMedica Limited	Devices and methods for the treatment of cancer	Europe	20-Feb-2002		Under examination
14/149881	Enigma Therapeutics Limited	Devices and methods for the treatment of cancer	USA	20-Feb-2002		Filed
4896740	pSiMedica Limited	New material and method of fabrication therefor	Japan	15-Dec-2004	06-Jan-2012	Granted
8293630	pSiMedica Limited	New material and method of fabrication therefor	USA	15-Dec-2004	23-Oct-2012	Granted
1704118	pSiMedica Limited	New material and method of fabrication therefor	Europe	15-Dec-2004	04-Dec-2012	Granted

Source: OncoSil Medical

## Board of Directors

### Mr Martin Rogers – Chairman

Martin Rogers is a startup investor and company director. Mr Rogers has experience in all aspects of financial, strategic and operational management and has helped raise over \$100m cash equity. Mr Rogers has been both an investor and senior executive in a private funded advisory business in the science and biotechnology sectors. Mr Rogers is also Chairman of Rhinomed Ltd (ASX:RNO), and non-executive director of Cellmid Ltd (ASX:CDY).

### Dr Neil Frazer – CEO and Managing Director

Dr. Frazer has been involved in drug and device development for over 27 years. He is a UK trained anaesthetist, and has worked for organizations such as Purdue Pharma, Glaxo and GlaxoWellcome, Shire Pharmaceuticals, Chimerix, Inc, Erimos Pharmaceuticals and Prima Biomed in senior management roles in the UK, the United States and in Australia. Dr. Frazer has been involved in the successful development of 10 new chemical entities over his career with the FDA and has a wealth of successful technical and commercial management.

### Dr Roger Aston – Non Executive Director

Dr. Aston has had extensive experience on boards of many pharmaceutical companies, and has been CEO of Pitney Pharmaceuticals Ltd, PSIMEDICA, PSIONCOLOGY PTE LTD, Peptech and Cambridge Antibody Technology. In 2001, he co-founded pSivida Limited. He served as the Chief Executive Officer of Hospira Australia Pty Ltd, and as Chief Executive Officer of Mayne Pharma Group Limited until February 15, 2012. He currently has several executive and non-executive board positions with prominent biotechnology companies.

### Mr Lawrence Gozlan – Non Executive Director

Mr Gozlan is the founder and Chief Investment Officer of specialised global life sciences investment fund, Scientia Capital. The business manages investments for high net worth individuals, family offices and institutional investors seeking exposure to the biotechnology industry. Prior to establishing Scientia Capital, Mr Gozlan managed Australia's largest biotechnology investment portfolio, as Queensland Investment Corporation's (QIC) institutional biotechnology analyst. He has also held roles with Foster Stockbroking, as the senior biotechnology analyst in the equities team and Deloitte, where he provided corporate advice for life science companies. Mr Gozlan is currently a non-executive director of Prana Biotechnology (ASX:PBT) and Phosphagenics (ASX:POH).

## Risks

There are a number of risks associated with an investment in **OncoSil Medical**, which are outlined below.

### Clinical Trial Failure

The major risk of the **OncoSil™** business is the risk of clinical failure in LAPC. Clinical failure can be defined as the risk that **OncoSil™** shows no benefit in OS, versus standard of care gemcitabine +/- Abraxane®. From a regulatory perspective, OS is the approveable primary endpoint in pancreatic cancer studies.

It is generally acknowledged by the medical community that extending overall survival (OS) by a meaningful amount (>2 months) is very challenging in this indication. This could be despite **OncoSil™** showing improvements in patient Quality of Life (QOL) measures including pain, and local tumour responses. Progression-free survival (PFS) in the pancreas would be the ideal primary endpoint, however, this endpoint is not registrable given most patients die from the disease invading local tissues and arteries and going metastatic.

### Reliance on One Technology, One Disease State

The **Company** is expected to derive all of its future revenues from a single product, **OncoSil™** in essentially one disease state, pancreatic cancer. Moreover, the technology should not be considered a mainstream treatment of widely disseminated metastatic disease, further limiting to the treatment to early stage, locally advanced disease patients. This constitutes a market of 28,084 patients in our view. There is a risk that despite clinical trials showing a benefit, the benefit is not sufficient enough to encourage adoption in its core market. As a result, the market may be considerably smaller than our assumptions suggest.

### Multiple Adoption Bottlenecks in Specialist Uptake

A major risk to the use of **OncoSil™** relates to the fact that pancreatic cancer is often managed via a multi-disciplinary team of specialists, as shown below.

The treatment of pancreatic cancer can be divided into several key specialities:

- (1) Surgery – pancreatic and hepatobiliary specialists
- (2) Minimally Invasive Surgery – interventional techniques into pancreas + surrounds (stents, drugs)
- (3) *Gastroenterology – required for OncoSil technique (patient referred by medical oncologist)*
- (4) *Medical Oncologists – prescribe chemotherapy, manage patient treatment*
- (5) Radiation Oncologists – deliver external beam radiation
- (6) Nuclear Medicine – required for **OncoSil™** product prep and delivery to theatre

We have identified two risk factors (shown in red) the first of which is the risk that medical oncologists are not adequately informed regarding the potential use of **OncoSil™** to drive patients into treatment by a

gastroenterologist, or due to the complexity of scheduling and management, referral becomes an overly burdensome deterrent. This was a major roadblock to early adoption of SIR-Spheres® in liver cancer.

The second relates to the training required for a gastroenterologist to perform the procedure. There are approximately 15,000 gastroenterologists practising in the US. However, gastroenterologists who perform advanced endoscopic procedures, such as endoscopic ultrasound (EUS) require additional training in therapeutic endoscopy as well as advanced training in hepatobiliary diseases, pancreatic diseases, and oncology. Moreover, given EUS has traditionally been used for defining tumour location, size and for biopsy, the deployment of **OncoSil™** would require an additional skill set. The American Society for Gastrointestinal Endoscopy (ASGE) represents this group.

### Limited Clinical Studies Exist

**Oncosil** has undertaken two pilot studies in locally advanced / metastatic pancreatic cancer, the results of which have been described. As a result, the **Company** is required to run major pivotal studies and as discussed there is a risk of failure. Moreover, the lack of a clinical program on a significant number of patients over the last six years (since 2008) may limit clinician interest/engagement in a new clinical program.

### Access to Capital

To date, **OSL** has raised approximately \$11.5m to fund its operations and to design a larger clinical trial. While the Company has indicated it is fully funded for a 150 patient study, there is a risk that further capital will be required in the event that a larger number of patients are required, or recruitment is slower than anticipated. There is a risk the **Company** may not be able to raise the requisite level of funds to undertake the necessary clinical program or to fund its operations.

### Regulatory/Reimbursement

**OSL** major market opportunity is in the US. The Centers for Medicare and Medicaid Services (CMS) pays for brachytherapy sources, including P<sup>32</sup>. However, these codes as discussed are not applicable to **OncoSil™** as a device. **OncoSil™** will be unable to leverage off any existing code. There is a risk that **OncoSil™** will not receive a code, and therefore limited/no reimbursement will be available. This is also true of the private payer market. As a result, patients will be required to pay for the procedure out of pocket. This will significantly limit sales in our view.

### Patent Protection

**OncoSil™** relies on patents and trademarks to protect its underlying competitive position in both the US and Europe. We have discussed the current patent position of the Company (above). We note the risk associated with progress patent expirations on the Company's ongoing competitive position. There is a risk that generic radiopharmaceutical competition may result, which seeks to cannibalise **OncoSil's** competitive position in pancreatic cancer, and potentially elsewhere (subject to further clinician uptake and clinical trials).

### Change in the Standard of Care for Pancreatic Cancer May Cause Obsolescence

There is a risk that newer chemotherapy agents progressively become approved in pancreatic cancer that could mean **Oncosil's** clinical trial in combination with gemcitabine and Abraxane® may no longer be a standard of care by the time **OncoSil™** is approved by the FDA in the US market. Given the lower hurdle for CE Mark for Class III devices, we see this scenario as unlikely. There is also a risk that radiotherapy techniques improve which provide better survival outcomes to patients.

We have examined the public databases for mid to late stage (Phase 2/3) pancreatic cancer studies. A total of 62 active clinical programs in locally advanced pancreatic cancer resulted from the search criteria. The majority of the studies are "tinkering" with current standard of care regimens, as outlined in Appendix 1 and 2. A number of studies are also investigating radiotherapy approaches in combination with chemotherapy, which as discussed above do not necessarily (to date) lead to improved survival outcomes.

As discussed, regosertib and TH-302 were the most advanced new therapies in clinical development; however in late CY13 regosertib in pancreatic cancer was discontinued.

## Reliance on Single Supplier, Single Source

The manufacturing, packaging and shipment of **OncoSil™** will most likely be the responsibility of Eckert & Ziegler under any final agreement signed. As a single supplier with manufacturing at a single source in Germany, there is a risk to global disruption of supply should Eckert be unable to manufacture. While several sources of manufacture may manifest in time, the reliance on one supplier is a risk. There is also a risk that margins will be impacted by the supplier raising the costs of manufacture/supply of **OncoSil™** or Eckert discontinue their contract with **OncoSil™** or cease manufacture.

## Outlook

Providing **OSL** leverages the innate flexibility in its design, based on the pilot studies and potentially a 15%+ interim PFS result, the product has sig. potential. The current trial design requires may be sufficient for a CE Mark in Europe for **OncoSil™**, but we do not believe it will satisfy US regulators via PMA. In our view, while a CE Mark is an attractive option, it will not guarantee sales without proven efficacy.

We therefore initiate coverage with a Speculative Buy and 12 month PT of \$0.26. Risks include slower than expected clinical trial recruitment, clinical trial failure, incremental benefit to SOC limiting use, changes in pancreatic cancer SOC over time, improvements in external beam radiation approaches, reimbursement, clinician training and adoption

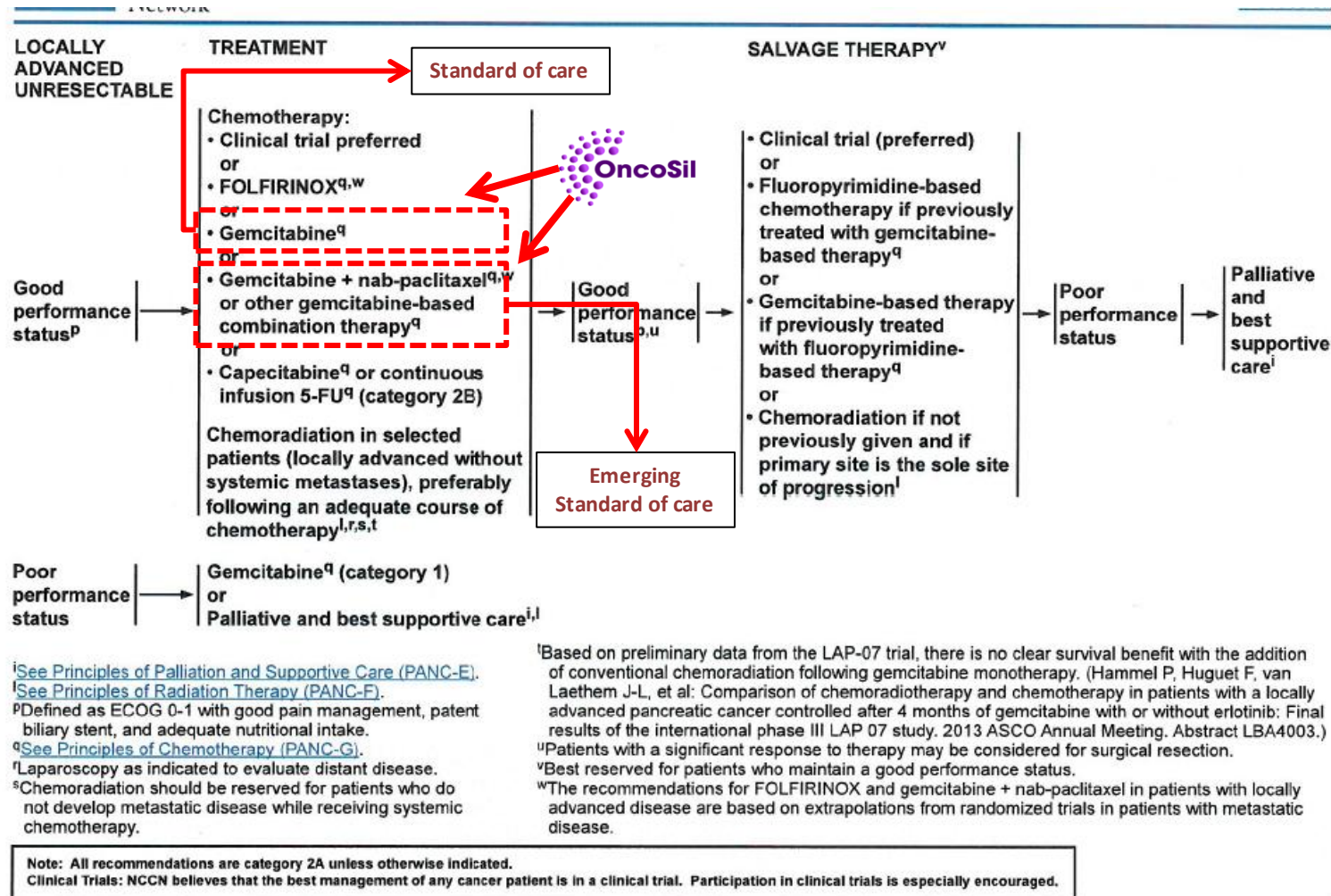
## APPENDIX 1 - ONCOSIL MARKET MODEL FOR UNRESECTABLE LAPC

Pancreatic Cancer Market Model	FY15	FY16	FY17	FY18	FY19	FY20	FY21	FY22	FY23	FY24	FY25	FY26	FY27	FY28	
	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	Estimate	
<b>United States</b>															
Incidence of Pancreatic Cancer	<b>45,220</b>	45,763	46,312	46,868	47,430	47,999	48,575	49,158	49,748	50,345	50,949	51,560	52,179	52,805	53,439
Incidence of Adenocarcinoma (95%)		43,475	43,996	44,524	45,058	45,599	46,146	46,700	47,260	47,828	48,402	48,982	49,570	50,165	50,767
Unresectable patients accessible at 85%		36,953	37,397	37,846	38,300	38,759	39,224	39,695	40,171	40,653	41,141	41,635	42,135	42,640	43,152
<b>Locally advanced patients at 47% occurrence</b>	<b>17,368</b>	<b>17,576</b>	<b>17,787</b>	<b>18,001</b>	<b>18,217</b>	<b>18,435</b>	<b>18,657</b>	<b>18,881</b>	<b>19,107</b>	<b>19,336</b>	<b>19,568</b>	<b>19,803</b>	<b>20,041</b>	<b>20,281</b>	
Unit Volumes	0	0	0	0	1,025	1,867	2,729	3,611	4,514	5,453	6,105	6,773	7,455	8,153	
<i>growth (%)</i>						82%	46%	32%	25%	21%	12%	11%	10%	9%	
<b>Basic Dosing Price (US\$'000/dose)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>12</b>	<b>12</b>	<b>12</b>	<b>12</b>	<b>12</b>	<b>12</b>	
Gross Sales (US\$'000) - single dose assumption	0	0	0	0	10,247	18,666	27,285	36,109	54,169	65,434	73,264	81,273	89,463	97,838	
Medical Device Tax - 2.3%	0	0	0	0	236	429	628	831	1,246	1,505	1,685	1,869	2,058	2,250	
Net Sales (US\$'000)	0	0	0	0	10,011	18,237	26,658	35,279	52,923	63,929	71,579	79,403	87,405	95,587	
Exchange Rate (USD/AUD)	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	1.09	
<b>Sales (A\$'000)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>10,912</b>	<b>19,878</b>	<b>29,057</b>	<b>38,454</b>	<b>57,686</b>	<b>69,683</b>	<b>78,021</b>	<b>86,550</b>	<b>95,271</b>	<b>104,190</b>	
<i>% of Global total</i>					60.9%	60.9%	60.9%	60.9%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	
<i>Implied patient penetration (doses)</i>					3.8%	6.8%	9.8%	12.8%	15.8%	18.8%	20.8%	22.8%	24.8%	26.8%	
<b>Europe (7)</b>															
Incidence of pancreatic cancer	<b>26,234</b>	26,549	26,867	27,190	27,516	27,846	28,180	28,519	28,861	29,207	29,558	29,912	30,271	30,635	31,002
Incidence of Adenocarcinoma (95%)		25,221	25,524	25,830	26,140	26,454	26,771	27,093	27,418	27,747	28,080	28,417	28,758	29,103	29,452
Unresectable patients accessible at 85%		21,438	21,695	21,956	22,219	22,486	22,756	23,029	23,305	23,585	23,868	24,154	24,444	24,737	25,034
<b>Locally advanced patients at 47% occurrence</b>	<b>10,076</b>	<b>10,197</b>	<b>10,319</b>	<b>10,443</b>	<b>10,568</b>	<b>10,695</b>	<b>10,824</b>	<b>10,953</b>	<b>11,085</b>	<b>11,218</b>	<b>11,352</b>	<b>11,489</b>	<b>11,627</b>	<b>11,766</b>	
Unit Volumes	0	0	0	0	594	1,083	1,583	2,095	2,619	3,163	3,542	3,929	4,325	4,730	
<i>growth (%)</i>						82%	46%	32%	25%	21%	12%	11%	10%	9%	
<b>Basic Dosing Price (EUR'000/dose)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>8</b>	<b>8</b>	<b>8</b>	<b>8</b>	<b>8</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	
Sales (EUR\$'000)	0	0	0	0	4,756	8,663	12,664	16,759	26,188	31,634	35,420	39,291	43,251	47,300	
Exchange Rate (EUR/AUD)	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	
<b>Sales (A\$'000)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>6,658</b>	<b>12,128</b>	<b>17,729</b>	<b>23,462</b>	<b>36,663</b>	<b>44,288</b>	<b>49,588</b>	<b>55,008</b>	<b>60,551</b>	<b>66,220</b>	
<i>% of Global total</i>					37.2%	37.2%	37.2%	37.2%	38.1%	38.1%	38.1%	38.1%	38.1%	38.1%	
<i>Implied patient penetration (doses)</i>					3.8%	6.8%	9.8%	12.8%	15.8%	18.8%	20.8%	22.8%	24.8%	26.8%	
<b>Australia</b>															
Incidence of Pancreatic Cancer	<b>2,546</b>	2,577	2,607	2,639	2,670	2,702	2,735	2,768	2,801	2,835	2,869	2,903	2,938	2,973	3,009
Incidence of Adenocarcinoma (95%)		2,448	2,477	2,507	2,537	2,567	2,598	2,629	2,661	2,693	2,725	2,758	2,791	2,824	2,858
Unresectable patients accessible at 85%		2,081	2,106	2,131	2,156	2,182	2,208	2,235	2,262	2,289	2,316	2,344	2,372	2,401	2,430
<b>Locally advanced patients at 47% occurrence</b>	<b>978</b>	<b>990</b>	<b>1,001</b>	<b>1,013</b>	<b>1,026</b>	<b>1,038</b>	<b>1,050</b>	<b>1,063</b>	<b>1,076</b>	<b>1,089</b>	<b>1,102</b>	<b>1,115</b>	<b>1,128</b>	<b>1,142</b>	
Unit Volumes	0	0	0	0	58	105	154	203	254	307	344	381	420	459	
<i>growth (%)</i>						82%	46%	32%	25%	21%	12%	11%	10%	9%	
<b>Basic Dosing Price (A\$'000/dose)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>6</b>	<b>6</b>	<b>6</b>	<b>6</b>	<b>6</b>	<b>7</b>	<b>7</b>	<b>7</b>	<b>7</b>	<b>7</b>	<b>7</b>	
<b>Sales (A\$'000)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>346</b>	<b>631</b>	<b>922</b>	<b>1,220</b>	<b>1,779</b>	<b>2,149</b>	<b>2,406</b>	<b>2,669</b>	<b>2,938</b>	<b>3,213</b>	
<i>% of Global total</i>					1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	
<i>Implied patient penetration (doses)</i>					3.8%	6.8%	9.8%	12.8%	15.8%	18.8%	20.8%	22.8%	24.8%	26.8%	
<b>TOTAL W/W Dose Sales</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1,677</b>	<b>3,055</b>	<b>4,465</b>	<b>5,909</b>	<b>7,387</b>	<b>8,923</b>	<b>9,991</b>	<b>11,083</b>	<b>12,200</b>	<b>13,342</b>	
<b>TOTAL W/W REVENUES (A\$'000)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>17,917</b>	<b>32,637</b>	<b>47,708</b>	<b>63,136</b>	<b>96,128</b>	<b>116,120</b>	<b>130,015</b>	<b>144,227</b>	<b>158,761</b>	<b>173,623</b>	
<i>Total Market (Eligible Patient) Penetration (%)</i>					3.8%	6.8%	9.8%	12.8%	15.8%	18.8%	20.8%	22.8%	24.8%	26.8%	

Source: Taylor Collison estimates

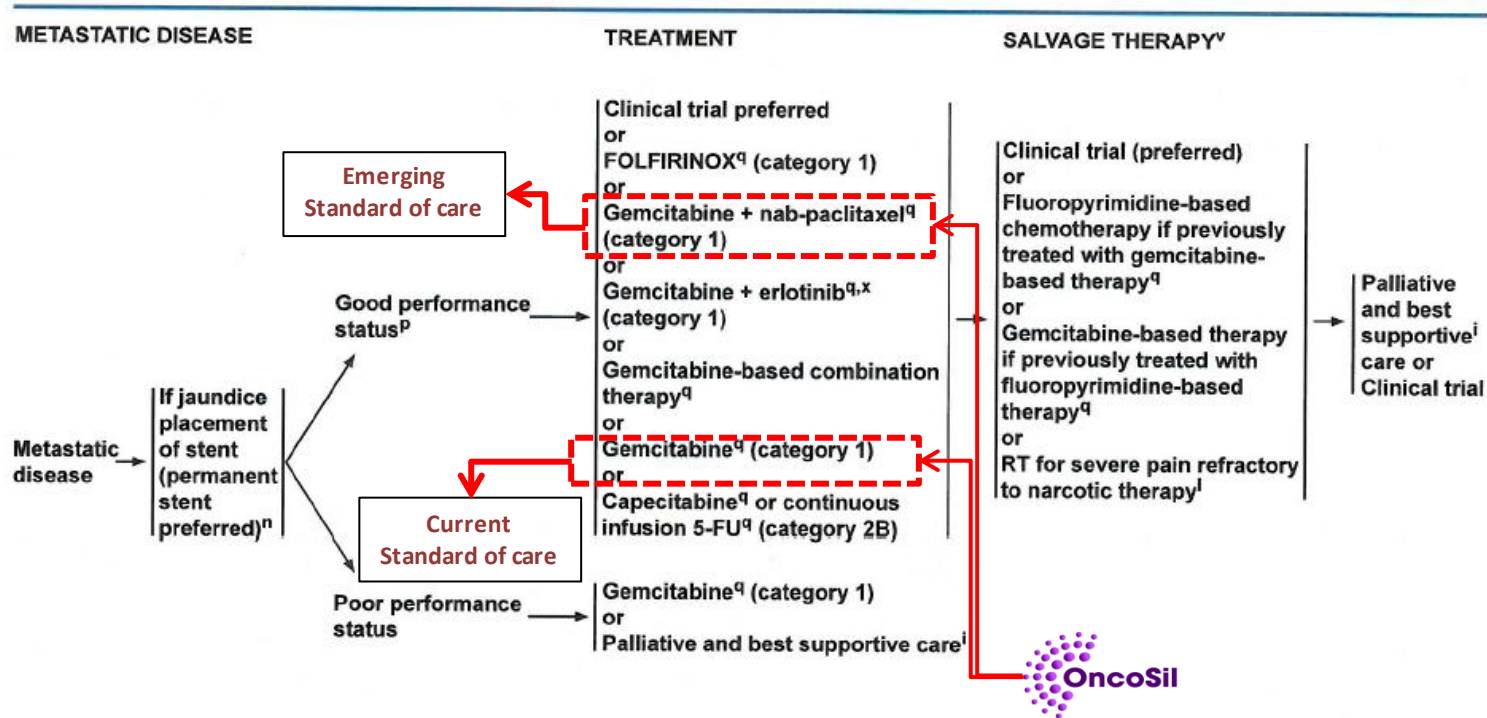
## APPENDIX 2

### NCCN TREATMENT SCHEMA: LOCALLY ADVANCED UNRESECTABLE PANCREATIC CANCER



Source: NCCN Guidelines, Taylor Collison

## APPENDIX 3 NCCN TREATMENT SCHEMA: METASTATIC PANCREATIC CANCER



<sup>l</sup>See Principles of Palliation and Supportive Care (PANC-E).

<sup>l</sup>See Principles of Radiation Therapy (PANC-F).

<sup>n</sup>Unless biliary bypass performed at time of laparoscopy or laparotomy.

<sup>p</sup>Defined as ECOG 0-1 with good pain management, patent biliary stent, and adequate nutritional intake.

<sup>q</sup>See Principles of Chemotherapy (PANC-G).

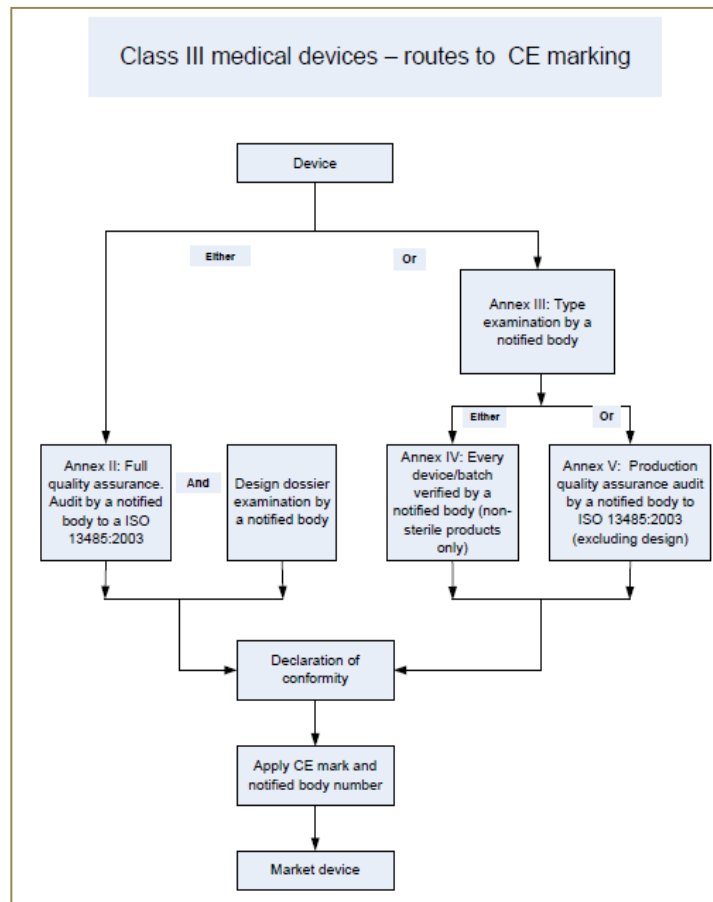
<sup>v</sup>Best reserved for patients who maintain a good performance status.

<sup>x</sup>Although this combination significantly improved survival, the actual benefit was small, suggesting that only a small subset of patients benefit.

**Note:** All recommendations are category 2A unless otherwise indicated.  
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.



### APPENDIX 4 – ROUTE FOR CE MARK (ONCOSIL), CLASS III



Source: MHRA UK

## ONCOSIL MEDICAL LIMITED - Summary of Forecasts

OSL \$ 0.145

PROFIT & LOSS SUMMARY (A\$'000s)				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
<b>Total Revenue</b>	<b>88</b>	<b>105</b>	<b>339</b>	<b>289</b>
<i>Growth (pcp)</i>	-	19.7%	221.9%	-14.8%
<b>EBITDA</b>	<b>(981)</b>	<b>(1,732)</b>	<b>(2,729)</b>	<b>(6,987)</b>
Dep'n/Other Amort'n	0	0	0	0
<b>EBIT</b>	<b>(981)</b>	<b>(1,732)</b>	<b>(2,729)</b>	<b>(6,987)</b>
Net Interest	100	105	339	289
<b>Pre- Tax Profit</b>	<b>(881)</b>	<b>(1,627)</b>	<b>(2,390)</b>	<b>(6,699)</b>
Tax Expense	0	0	0	0
Minorities	0	0	0	0
<b>NPAT</b>	<b>(881)</b>	<b>(1,627)</b>	<b>(2,390)</b>	<b>(6,699)</b>
<i>Growth (pcp)</i>	-	84.7%	46.9%	180.2%
Adjustments	0	0	0	0
NPAT Reported	(881)	(1,627)	(2,390)	(6,699)

PER SHARE DATA*				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
<b>EPS (c) - Reported</b>	<b>(0.3)</b>	<b>(0.5)</b>	<b>(0.7)</b>	<b>(1.9)</b>
<i>Growth (pcp)</i>	-	84.7%	46.9%	180.2%
<b>EPS (c) - Adjusted</b>	<b>(0.3)</b>	<b>(0.5)</b>	<b>(0.7)</b>	<b>(1.9)</b>
<i>Growth (pcp)</i>	-	84.7%	46.9%	180.2%
Gross CF per share (c)	(0.3)	(0.2)	(0.5)	(1.6)
NTA per share (c)	1.0	3.0	2.3	6.1
Dividend (c)	0.0	0.0	0.0	0.0
Franking	-	0%	0%	0%

KEY RATIOS				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
Current ratio (x)	18.6	11.6	5.8	8.4
Net Debt : Equity (%)	-58.0%	-86.6%	-91.1%	-100.5%
Net Debt: EBITDA (x)	3.6	6.5	3.5	3.4
ROE (%)	-29.1%	-17.0%	-20.2%	-38.9%
ROIC (%)	-34.7%	-65.7%	-179.7%	4186.1%
Dividend Payout Ratio (%)	n/a	n/a	n/a	n/a

VALUATION MULTIPLES				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
<b>Reported PE Ratio (x)</b>	<b>n/a</b>	<b>n/a</b>	<b>n/a</b>	<b>n/a</b>
<b>Adjusted PE Ratio (x)</b>	<b>n/a</b>	<b>n/a</b>	<b>n/a</b>	<b>n/a</b>
Dividend Yield (%)	0.0%	0.0%	0.0%	0.0%
EV/Sales (x)	n/a	n/a	n/a	n/a
EV/EBITDA (x)	n/a	n/a	n/a	n/a
EV/EBIT (x)	n/a	n/a	n/a	n/a

CAPITAL RAISING ASSUMPTIONS				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
Shares Issued (m)	0.0	79.2	0.0	100.0
Issue Price (A\$)	0.00	0.13	0.00	0.20
Cash Raised (A\$m)	0.0	10.3	0.0	20.0

BALANCE SHEET SUMMARY				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
Cash	3,511	11,301	9,627	24,029
Receivables	14	17	54	46
Inventories	0	0	0	0
Other	10	10	10	10
<b>Total Current Assets</b>	<b>3,592</b>	<b>11,385</b>	<b>9,747</b>	<b>24,142</b>
Inventories	0	0	0	0
PP&E	3	103	203	303
Intangibles	2,648	2,648	2,648	2,648
Other	0	0	0	0
<b>Total Non- Current Assets</b>	<b>2,651</b>	<b>2,751</b>	<b>2,851</b>	<b>2,951</b>
<b>TOTAL ASSETS</b>	<b>6,243</b>	<b>14,136</b>	<b>12,598</b>	<b>27,093</b>
Accounts Payable	54	843	1,695	2,888
Borrowings	0	0	0	0
Provisions	0	0	0	0
Other	139	139	0	0
<b>Total Current Liab</b>	<b>193</b>	<b>982</b>	<b>1,695</b>	<b>2,888</b>
Borrowings	0	0	0	0
Provisions	0	105	339	289
Other	0	0	0	0
<b>Total Non- Current Liab</b>	<b>0</b>	<b>105</b>	<b>339</b>	<b>289</b>
<b>TOTAL LIABILITIES</b>	<b>193</b>	<b>1,087</b>	<b>2,034</b>	<b>3,177</b>
<b>TOTAL EQUITY</b>	<b>6,050</b>	<b>13,049</b>	<b>10,564</b>	<b>23,916</b>

CASH FLOW SUMMARY				
Period	FY 13 A	FY 14 E	FY 15 E	FY 16 E
<b>EBIT (excl Abs/Extr)</b>	<b>(981)</b>	<b>(1,732)</b>	<b>(2,729)</b>	<b>(6,987)</b>
Add: Dep'n & Amort'n	0	0	0	0
Change in Pay.	(47)	789	853	1,193
Less: Tax paid	0	0	0	0
Net Interest	114	105	339	289
Change in Rec.	(9)	(3)	(37)	8
Change in Inv.	0	0	0	0
<b>Gross Cashflows</b>	<b>(923)</b>	<b>(841)</b>	<b>(1,575)</b>	<b>(5,498)</b>
Capex	(4)	(100)	(100)	(100)
<b>Free Cashflows</b>	<b>(927)</b>	<b>(941)</b>	<b>(1,675)</b>	<b>(5,598)</b>
Share Issue Proceeds	0	11,454	0	20,000
Other	2,026	0	0	0
Dividends Paid	0	0	0	0
<b>Net Cash Flow</b>	<b>1,099</b>	<b>10,513</b>	<b>(1,675)</b>	<b>14,402</b>
FX Effect on Cash	0	0	0	0

OSL - VALUATION METHODOLOGY				
	Multiple	Weight (%)	Valuation (A\$ ps)	Blended Valuation (\$ps)
rDCF (WACC 17.5%)	n/a	33.3%	\$0.19	\$0.07
Disc. P/E Valuation	20x FY19	33.3%	\$0.34	\$0.11
Disc. EV/EBITDA Valuation	15x FY19	33.3%	\$0.24	\$0.08
<b>Blended Equity Valuation</b>				<b>\$0.26</b>

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