

## Diversifying portfolio spreads the risk

16 September, 2016

SalvaRx's (SALV) long term aim is to develop a pipeline of complementary cancer immunotherapy-focused products and technologies, activating the body's immune system to down-regulate tumour progression. Achieving a durable patient response to support long-term survival is essential for Pharma companies scouting new clinical assets. SALV's expanding product portfolio continues to create a substantial licensing or exit opportunity for investors.

### US\$2m investment in Intensity Therapeutics

Broadening its portfolio with a \$2m stake in Intensity (8.5% equity) provides access to a novel cancer drug delivery platform, **DfuseRx**, that not only **destroys primary tumours in preclinical models**, but also **stimulates a potent systemic T-cell response** for long-term immune-based protection.

### iOx Therapeutics to access Horizon 2020 grant, worth >€8m

iOx is a member of an international multi-discipline consortium which is set to use the grant money to support the development of new immunotherapy candidates.

- **Intensity Therapeutics aims to enter the clinic before YE** and is preparing submissions for INT230-6, its lead therapy, to commence clinical trials in the US and Canada.
- **INT230-6 is a potential endogenous tumour immunotherapy:** Results from preclinical models have demonstrated a strong efficacy against the primary tumour - avoiding usual toxic systemic effects of chemotherapy - and stimulating a potent immune response to help combat distal/metastatic tumours.
- **iOx expands pipeline through access to grant funding:** With Horizon 2020 funding, iOx is to combine its lead IMM60 with a therapeutic vaccine (NY-ESO-1), in a novel nanoparticle formulation (IMM65), in various solid tumours.
- **iOx evaluating novel nanoparticles to enhance immune response:** Various studies suggest that a coordinated release (of antigens and other immune system stimulating agents) from a nanoparticle formulation induces a stronger T-cell response. A positive clinical demonstration could represent a new platform for creating therapy combinations, particularly with vaccines.
- **Speculative, but highly attractive investment segment.** The cancer immunotherapy segment has become a focus of attention for industry M&A, with high-value deals (some >\$1bn) - even for preclinical programmes. The opportunity for SALV investors to exit on a premium multiple continues to be a realistic prospect.
- **Substantial preclinical efforts and progress** made following the IPO indicate **strong value creation**. SALV continues to identify strategic assets to invest in, or acquire, with a mission to bring novel immunotherapy treatments for cancer treatment through development.

### Company Data

EPIC	AIM:SALV
Price (last close)	28.5p
52 week Hi/Lo	36p / 23p
Market cap	£10.4m

### Share Price, p



Source: ADVFN

### Description

SALV invests in novel cancer immunotherapies. Its portfolio companies include iOx Therapeutics and Intensity Therapeutics Inc. The company aims to help develop new anti-cancer therapies, benefitting from substantial value creation through to proof-of-concept and the significant escalation of pharmaceutical M&A activity in the immuno-oncology sector.

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## Executive summary

**The SALV business model is focused on investing in and developing novel mechanism-driven immunotherapies. Cancer is the 'hottest' area of drug development,** with the immunotherapy segment currently enjoying the limelight. Immunology has promoted a step-change in therapy effectiveness in the clinic, which has translated to strong share price evolution for those companies developing new cancer immunotherapy products with blockbuster commercial potential.

**SALV has progressed its buy & build strategy,** designed to complement the emerging 'checkpoint-enhanced' standard of cancer care with additional 'novel mechanism of action' products. Today, SALV has the cornerstone of a diversified portfolio of clinical assets.

**SALV's commercial opportunity** is to develop an expanded and robust pipeline, acquiring novel and differentiated anti-cancer assets that are potentially complementary to existing anti-cancer therapy products and, preferably, synergistic in activity.

iOx Therapeutics is seeking new drug candidates that can **modulate the body's 'innate' immune response** (and also link with the 'adaptive' arm) producing a unique and differentiated approach. **If iNKT cell activation potentially expands** to become anywhere near as key to oncology treatments as some of its counterparts (i.e. PD-1 inhibitors), then companies with the **lead drug candidates could be set for a big payday.**

SALV's **\$2m investment in Intensity Therapeutics** support efforts to destroy primary tumours and also turbo-boost the tumour antigen 'presentation' to the immune system, enhancing the efficiency of CD8+ (tumour specific) T-cell generation (so-called 'killer T-cells'). Intensity's platform represents, in part, a novel approach to stimulate an effective response from the immune system's 'adaptive' arm.

Current development efforts should move into the clinic shortly (**Phase 1/2 study with iOx's IMM60,** alone and in combination with an approved 'checkpoint inhibitor'; **Phase 1/2 study with Intensity's INT230-6,** again alone and in combination with a PD-1 inhibitor). Positive outcomes could suggest a generic treatment approach, in each case, for combining with a spectrum of approved and in-development 'checkpoint' inhibitors.

**Cancer immunotherapy** is a relatively new field but quickly gaining clinical support and commercial traction, with a **market projection of >\$70bn sales by 2020** (Source: *Research&Markets.com*).

Positive results from SALV's initial trials are likely to attract the interest of the pharmaceutical industry's oncology strategy and business development teams. With the recent trend to underpin M&A and licensing deals with significant monetary terms (that have already reached >\$1bn for just preclinical assets), the opportunity for investors in SALV to **exit on a premium multiple should be a realistic prospect.**

## SalvaRx's investment opportunity

SalvaRx Group plc (SALV) is a life sciences development company investing in innovative technology platforms to deliver new anti-cancer drugs in the immunotherapy space with novel mechanisms of action. Cancer immunotherapy is a relatively new field but as already stated is rapidly building scale and momentum.

An investment in SALV represents an opportunity to participate in the exciting, fast-growing and, importantly, commercially viable cancer treatment segment of immunotherapy. These newer cancer treatments and, particularly in combination approaches, suggest that harnessing the body's immune system can produce the most durable results and improved patient survival.

**iOx Therapeutics** (SALV invested £0.5m, and committed to a further ~£1.3m) is about to enter clinical development with its first product, IMM60, that aims to stimulate a specific immune cell (Natural Killer T-cell or NKT cell) to potentially up-regulate its activity against tumour cells.

An initial Phase 1/2 study should determine IMM60's activity alone and in combination with an approved 'checkpoint inhibitor' - a positive result would suggest that this approach could work generically with a spectrum of approved and in-development 'checkpoint' and other cancer pathway-inhibitor drug molecules and (potentially) vaccines.

The recent \$2m investment in **Intensity Therapeutics** and the **Horizon 2020 grant award** represent very encouraging progress within the stated strategy. Intensity aims to commence a Phase 1/2 study with its lead, INT230-6, in a number of solid tumours before year-end. The Horizon 2020 consortium work is a development project with the aim, amongst other things, to assess IMM65 (a combination of IMM60 with a recognised therapeutic vaccine) and to evaluate a novel nanoparticle formulation approach to enhance immune system stimulation.

As these anti-cancer 'assets' are developed, the utility of bringing (multiple) novel mechanism approaches, in potential (multi-)combination therapies using cytotoxic, biological, immune response modifiers and cellular approaches is likely to also **elicit great interest from the Pharma oncology industry.**

**SALV's strategy is to build a diverse portfolio, or pipeline of assets,** through investment in companies with innovative development programmes, exceptional management and outstanding growth opportunities. A key focus is on cancer and immunology, emphasised by its initial investment.

In our opinion, this **diversified portfolio** (focused on immunotherapy), under expert scientific and commercial management, and financially supported by own resources (relatively limited) but more substantial partner and non-dilutive funding, represents an exciting opportunity to invest in the life sciences sector.

## Catalysts

We have identified some near-term potential events that could result in share price moves:

Potential 'trigger' events		
Calendar		Event
2016	✓	Decision made on IMM60 drug product manufacturing plan
2016	✓	Nominate a second iOx product for the clinic
2016	✓	Potential second transaction for SALV (Intensity Therapeutics)
2016		Commence human study with INT230-6 (in various solid tumours)
2017		Commence human study with IMM60 (in metastatic melanoma)

Source: Company

## Investment Risks

We believe the main uncertainties in SALV's commercial ambitions relate to:

- In the near term, a lack of efficacy and little activity differentiation with iOx NKT agonists or, separately, novel DfuseRx formulations from Intensity's pipeline, either alone, or in combination with PD-1 and/or other checkpoint inhibitors;
- Material delays in eliciting interest and establishing iNKT and/or DfuseRx development licences with pharmaceutical partners and other commercial partners;
- Lack of investor commitment to invest in additional funding rounds;
- In the medium term, failure to identify acquisition targets or obtain additional funding to follow a 'buy & build' model; and
- Potential product competition, new technology entrants.

## Investment portfolio

Since we initiated coverage on SALV in March 2016 the company has made substantial progress, including:

- Investing US\$2m in Intensity Therapeutics (private) for a 8.5% equity interest,
- iOx Therapeutics has been granted a US patent (covers its IMM6 product - alone and in combinations),
- Gained access to Horizon 2020 grant funding of >€8m (as part of an international consortium),
- IMM60 is set to commence a human study in 2017,
- Currently preparing initial clinical trial applications (US FDA, Health Canada) for Intensity's lead product, INT230-6.

SALV has a 60.5% interest in iOx Therapeutics, which has two products under development, with one, IMM60, likely to move into the clinic next year.

SALV invested \$2m in Intensity Therapeutics' Series A round for \$10m earlier this year (for an 8.5% equity interest), and this company's lead product, INT230-6, could enter the clinic before year-end.

Looking forward, we understand that SALV is **actively screening for further acquisitions or investments** in cancer immunotherapy and other, complementary areas of oncology.

SALV had cash resources of £0.9m at 31 Dec 2015. In order to facilitate the investment in intensity, the company issued \$1m of zero coupon convertible unsecured loan notes to two senior SALV directors, Jim Mellon and Greg Bailey. The loan notes have a term of 3 years.

It's also worth noting that SALV has been able to secure collaborative research support and grants, **equivalent to ~£20m (and all non-dilutive)**, for its two iOx programmes (IMM60 and IMM65).

## iOx Therapeutics

As a reminder, iOx Therapeutics (iOx) was founded in February 2015 by ISIS (Oxford University's technology transfer arm) and the Ludwig Institute. The aim is to develop a new type of immunotherapy against cancer, using key findings from an earlier collaboration between Professor Vincenzo Cerundolo (of Oxford University) and the Ludwig Institute.

iOx's team discovered a number of synthetic lipid compounds that were found to activate iNKT cells and potentially play an important role in anti-cancer immune responses. Oxford University's Weatherall Institute of Molecular Medicine has been working on the biology of iNKT cells for >10 years. These synthetic lipid compounds form the basis of iOx's R&D programme. iOx has an exclusive licence (with the right to sub-licence) from the Ludwig Institute to develop and commercialise iNKT cell agonists (including IMM60) for treating various human diseases, including cancer. iOx was recently granted a US patent on IMM60 for use as a standalone anti-cancer treatment, as well as in combination with a tumour vaccine (co-formulation) or with immunotherapy agents (such as PD-1 inhibitors).

iOx is aiming to carry out a **~60-patient study of IMM60 in advanced melanoma**. Preliminary discussions with the UK's Medical and Healthcare products Regulatory Agency (MHRA) have taken place regarding trial design, although the protocol has yet to be finalised. This study is to be fully funded by Oxford University. As previously mentioned, we understand that the combined Phase 1/2 study is likely to include:

- **A dose-finding study** in order to establish some clinical parameters for IMM60 alone and in combination with a PD-1 inhibitor (includes maximum tolerated dose, MTD and any dose-limiting toxicity, DLT), followed by a
- **3-arm randomised study** of IMM60 alone, compared to the PD-1 inhibitor alone, and compared to the combination of IMM60 and the PD-1 inhibitor.

**The aim is to develop an immunotherapy product that can achieve a significant long-term response (a 'functional cure') in multiple cancer types, helping improve overall survival.**

Additional studies are being considered in lung cancer (IMM60, preclinical status) and as a vaccine adjuvant (IMM47, preclinical status). Further agonist candidates are at the discovery stage.

#### Summary of clinical assets in portfolio companies

	Product	Indication area(s)	Details	Administration route	Status
<b>iOx Therapeutics (SALV has a 60.5% equity interest)</b>	<b>IMM60</b>	malignant melanoma (lung cancer - preclinical)	One of a series of non-glycosidic agonists based on threitolceramide (ThrCer)	via liposomal administration	Phase 1/2 human trial to start in 2017. Treatment is with IMM60 alone and combined with a PD-1 inhibitor
	<b>IMM65 (IMM60 co-formulated with NY-ESO-1 vaccine)</b>	Various solid tumours (bladder, ovarian, lung & others)	A co-formulation consisting of IMM60 and NY-ESO-1, a therapeutic vaccine (the NY-ESO-1 antigen was discovered by the Ludwig Institute)	Investigating a potential co-administration using PLGA (poly-lactic-co-glycolic) nanoparticles; also investigate injection into lymph nodes versus IV admin	In development (funded by the Horizon 2020 award grant). Treatment is to be with IMM65 alone and combined with a PD-1 inhibitor Preclinical
	<b>IMM47</b>	As a vaccine adjuvant			
<b>Intensity Therapeutics (SALV has an 8.5% equity interest)</b>	<b>INT230-6</b>	Melanoma (initially), progressing to 'deeper-seated' solid tumour locations	A combination of cisplatin, vinblastine with an amphiphilic cell penetration enhancer excipient	Intra-tumoral instillation (using a device approved in US/EU)	Phase 1/2 human trial to start in 2016. Treatment is (potentially) in combination with PD-1 and/or PD-

Source: Company

## Intensity Therapeutics Inc.

Intensity Therapeutics (IT) was founded in 2012, pioneering a **novel approach to treating solid tumours**. The company's DfuseRx platform technology is able to rapidly profile current therapeutic agents, to identify cell 'penetration enhancers' that match a particular drug to a cell type, and potentially improve the efficacy of the new Intensity formulation.

Following direct injection into the tumour, this approach potentially increases the intracellular concentration of the active drug in the tumour to a toxic level, without exposing the rest of the body to a similarly high concentration of the drug. **This technique has a bonus**. Direct injection of the enhanced formulation can kill the primary tumour. Furthermore, in-situ tumour destruction helps improve the presentation of tumour cell antigen(s) to the immune system.

Intensity's preclinical studies with its lead product, INT230-6, have demonstrated strong efficacy against the primary tumour without the systemic distribution and toxic effects normally observed with these anti-cancer drugs. Furthermore, INT230-6 has also effected a vigorous systemic immune response, sufficient to affect distal and metastatic tumours (see later).

An IND (Investigational New Drug) application is being prepared for the US FDA and a clinical trial application (CTA) for Health Canada, with the intention to move into the clinic before year-end. Ian Walters, SALV's CEO, has been working with Intensity as its Chief Medical Officer since 2014.

## Consortium tapping Horizon 2020 grant for >€8m

An international multi-disciplinary consortium of 11 academic and commercial partners (including iOx Therapeutics) has been awarded an **€8.3m Horizon 2020 grant** to support new immunotherapy development.

One of the drug candidates being developed is a combination product based on one of iOx's compounds - IMM65 is a combination of IMM60 and the Ludwig Institute for Cancer Research's NY-ES0-1 tumour vaccine. Furthermore, the grant funding is to help establish the advantages (if any) of administering the combination as a 'nanoparticle'.

**Encapsulation of antigens and immune-stimulating agents has been shown to enhance the stimulation of anti-tumour immunity**. Preliminary studies by researchers (including Vincenzo Cerundolo's group at Oxford University) have demonstrated the coordinated release and delivery of an **antigen and agent** 'payload' and a greater induction of antigen-specific T-cells. Furthermore, iOx has identified **selected non-glycosidic iNKT cell agonists** (based on threitolceramide, ThrCer) that, in combination with protein antigen, help stimulate (antigen-specific) cytotoxic T lymphocytes without the requirement for CD4 T-helper cell assistance and also produce large amounts of IFN- $\gamma$  (interferon-gamma, which helps activate a broad spectrum of immune cells to fight tumour cells).

More precisely, co-encapsulation of the antigens provided the best results. In preclinical studies, a single immunisation with a 'protein antigen'/  $\alpha$ -GalCer nanoparticle was able to induce a substantial protection from tumour formation - and even delayed the growth of established tumours - which coincided with a much enhanced antigen-specific CD8+ T cell response (more recent iOx work is investigating ThrCer variants).

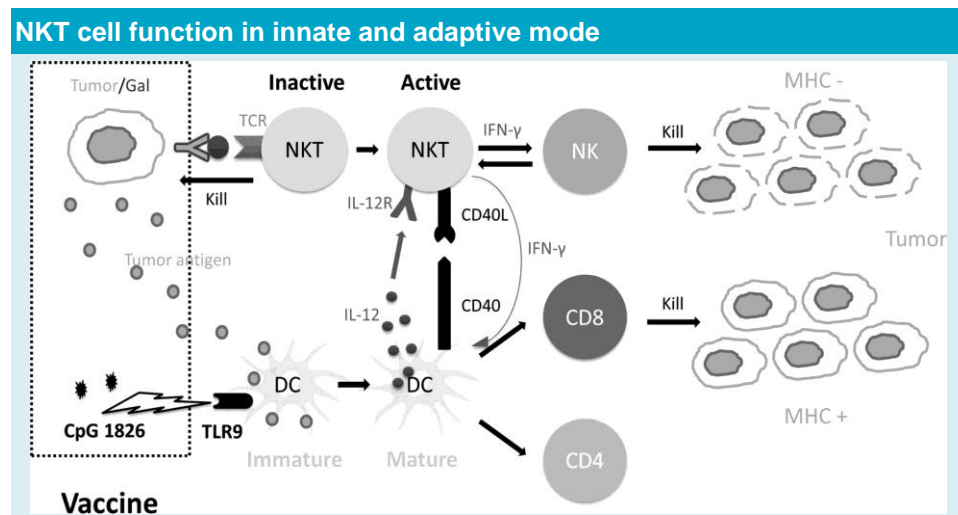
## Cancer treatment is evolving

In our last note (March 2016), we focused on iOx's progress in stimulating the induction and activation of iNKT cells. iOx is seeking **new drug candidates that can modulate the body's 'innate' immune response** (and also link with the 'adaptive' arm) producing a unique and differentiated approach.

As a reminder, these are the *invariant* NKT, or iNKT cells (a subset of the NKT cell population - see initiation report for details). Their activation can be caused by a range of stimuli, antigenic or chemical, and through interaction with other immune cells (like antigen presenting cells, APC) providing a watchdog function in the immune surveillance for 'non-self' across the body's immune system. **iNKT cells can respond to these stimuli** - including non-self tumour antigens - **extremely fast**, secreting chemicals to attack bacteria, viruses and tumour cells, as well as linking into the adaptive immune arm (to potentiate CD8+ killing).

**NKT cells 'punch well above their weight'**, with antigen recognition to both self- and non-self antigens (unlike other T-cells) and fast reaction to stimulation through producing a range of cytokines and chemokines to modulate the immune response. This modulation can have both immune-enhancing and immuno-suppressive effects.

On stimulation, NKT cells produce a range of cytokines including interferon (IF)-gamma, interleukins (ILs-2, -4, -10, -13, -17, -21 and -22), GM-CSF and TNF-alpha. These cytokines activate other immune cells (NK cells, T cells and B cells) to help recruit additional cytolytic cells for tumour surveillance. At the same time, dendritic cell (DC) maturation (through NKT activation) potentiates CD8+ T cells. **These are cytotoxic T-cells that can kill tumour cells.**



Source: Dong et al, Co-operation of  $\alpha$ -galactosylceramide-loaded tumour cells and TLR9 agonists induce potent anti-tumour responses in a murine colon cancer model, *Biochem J* (2015)

Representation of this complex interplay and the constant new detail that is becoming apparent through research efforts (at Oxford University and other institutions) is difficult.

Nevertheless, the activation of NKT cells through presentation with tumour antigens and depiction of the immediate and subsequent killing efforts directed at the tumour cells by cytokines (amongst others) or indirectly through interaction with DC to further activate more professional and long-lived killer T-cells, particularly CD8+, is simplified as shown above.

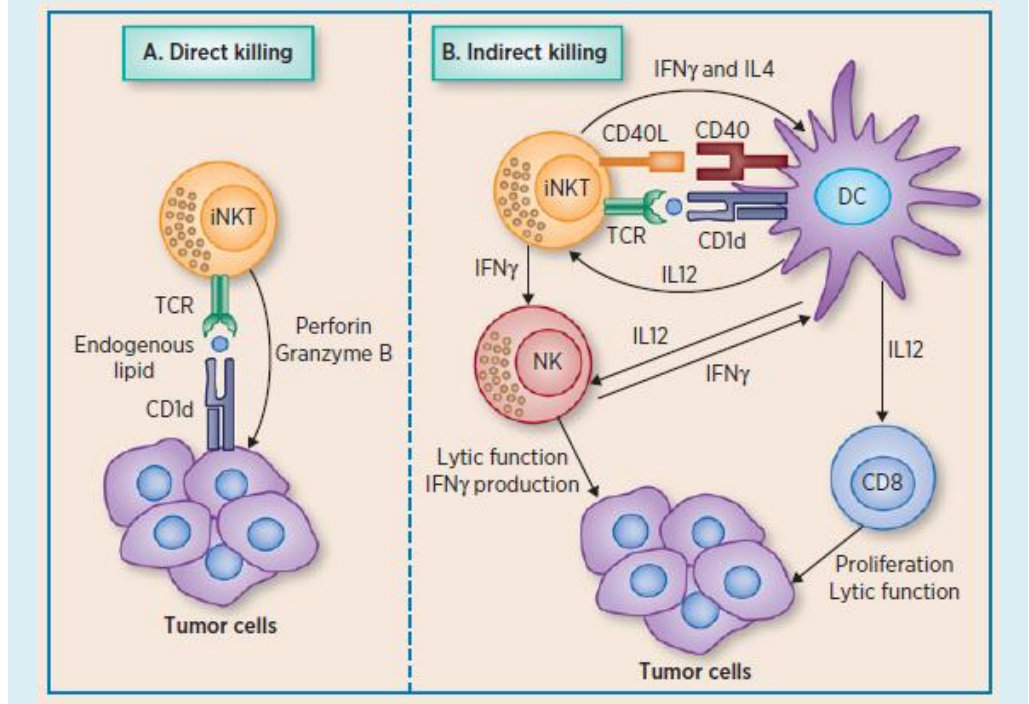


### iOx's iNKT programme

The proposed combined Phase 1/2 study is likely to focus on combining the iNKT agonist, IMM60, with an approved PD-1 class inhibitor (which could be either nivolumab or pembrolizumab).

A potential successful outcome to this trial would establish a meaningful difference between the separate monotherapy arms and the combined arm, **suggesting activation of NKT cells and potentiation of both the target cellular networks**. Further work is likely to be needed to distinguish direct from indirect immune system effects, but the significance of such an outcome, albeit preliminary, would resonate strongly with pharmaceutical companies on the look-out for novel and effective cancer immunotherapy assets.

#### Anti-tumour activities of iNKT cells



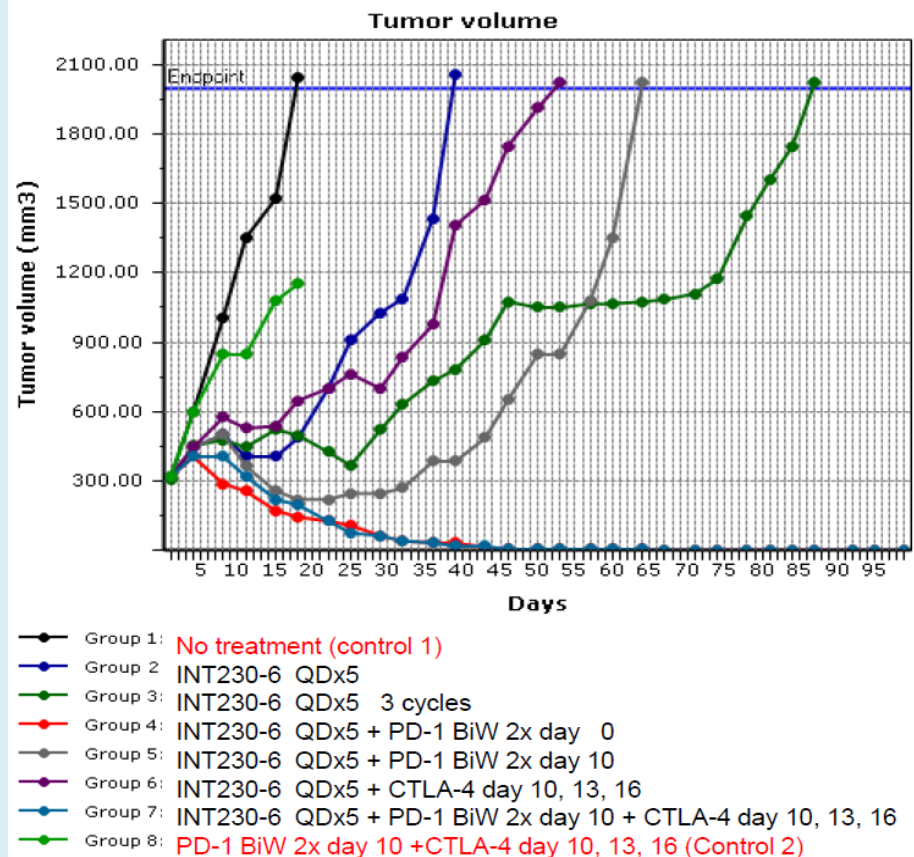
Source: McEwen-Smith et al, *Cancer Immunol Res*, American Association for Cancer Research 2015. Direct Killing - recognition of CD1d-presented tumour antigens, followed by iNKT cell-mediated lysis, or Indirect Killing - CD1d-expressing and TLR (Toll-like receptor)-activated APC (Antigen Presenting Cell) promotes activation of NK (Natural Killer) cells and tumour-specific T-cell response leading to indirect tumour cell death.

## Intensity's DfuseRx programme - INT230-6

INT230-6 is a combination of cisplatin, vinblastine and an amphiphilic cell penetration excipient. Injected directly into established (colon cell line) tumours (that is, intra-tumour) in mice resulted in rapid shrinkage of the injected tumours. In summary, initial preclinical results of the INT230-6 formulation can be summarised as follows:

- **Improved drug diffusion and uptake** into the cancer cell;
- **More rapid and improved drug penetration through the tumour** - including hypoxic and un-vascularised regions;
- **Long-lived tumour shrinkage effect** (past multiples of chemotherapy half life - implies more than just a direct chemo effect);
- **Significant extension of overall survival** compared to controls;
- **Resistance to re-inoculation with colon cancer cells** by complete responder animals - and apparent tumour immunity persisted for >1 year (potential permanent immunity);
- **Shrinking tumours showed an influx of T-cells and DC** (presumably to process the released antigens and help induce immunity).

### INT230-6 activity alone, in multiple cycles and with PD-1 or CTLA-4



Source: Bloom, A, Bender L, Terabe M, Berzofsky J, Walters I (2015), poster presentation, 30th Annual Meeting Society for Immunotherapy of Cancer. Novel drug INT230-6 shows strong synergy with anti-PD-1 antibodies and can induce high complete response rates with T-cell memory response in a colon cancer mouse model.

Separate, but similar, studies have confirmed additional benefits for INT230-6 that, if replicated in initial human studies, could point to this product not only acting as a novel immunotherapy but also as an endogenous tumour vaccine.

- CD4- and CD8-depletion studies suggested that the **initial shrinkage in tumour mass was primarily due to the chemo drugs** (in the INT230-6), but **a complete response required induction of CD8 T cells**.
- Investigating the long-lived immunity aspect, **re-challenge of complete responder mice** (alongside CD4- and CD-8 depletion) suggested that INT230-6 **induced a CD4- and CD8-dependent immunological memory**.
- Induction of memory was important in controlling recurrence **as well as controlling tumours at distant sites**; and
- Combined with checkpoint inhibitors in a similar mice model, either PD-1 (biweekly for 2 weeks) or CTLA-4 (3 doses, 3 days apart), given intra-peritoneally 10 days post the first INT230-6 dose, **survival was extended**. Untreated mice survived for <25 days; addition of checkpoint inhibitors enhanced the 10% complete response (CR) obtained with INT230-6 alone. A combination of all three enabled a 50% CR. **Most interestingly, simultaneous administration of INT230-6 and PD-1 produced a 50% CR (without CTLA-4)**.

## SalvaRx's commercial opportunity

Although (some) immunotherapies have been around for years (importantly cytokines and a variety of targeted antibody therapies), **heightened commercial interest has significantly increased following successful and highly encouraging trial outcomes with (especially) PD-1** (and other checkpoint) inhibitors, as well as for alternative immunotherapeutic approaches.

A wave of **new concept-based immunotherapy agents** hold out the promise of improved survival with lower toxicity for some patients. At the same time, combination therapies address multiple pathways in a tumour, potentially leading to substantial increases in survival.

**Targeted therapies now account for almost 50% of total spending** on oncology drugs and they have been growing at a compound average growth rate of 14.6% over the past five years. More specifically, the immunotherapy drugs market is estimated to grow at a CAGR of 12.8% to reach >\$70bn by 2020 (Markets&markets.com, 2015). **The checkpoint inhibitors, by type of drugs, are expected to witness the fastest growth during this period.**

SALV currently has no product sales or meaningful revenues. However, and as we have noted, the company has a number of potential technology opportunities (iOx Therapeutics, Intensity Therapeutics and the Horizon 2020 consortium) with various potential future revenue streams that should, in time, allow us to develop a detailed earnings model.

**As we have previously emphasised, the market opportunity is a significant and rapidly growing one.** The impact of iOx and Intensity's product candidates (as part of separate oncology combination therapies) on human health could be huge, allowing SALV multiple entry tickets into licensing discussions with pharmaceutical companies and biotech companies.

There are, nevertheless, a number of potential risks to manage and overcome - **a major challenge will be to prove that such therapies represent an improvement over current treatments**, with well-designed and controlled clinical trials that demonstrate a superior long-term efficacy and safety (to current pharmacotherapy).

**The commercial goal** is a deal (preferably following the planned, proof of concept Phase 1/2 studies) which could be either a license and development agreement, product acquisition or sale of the company. The oncology immuno-chemotherapy segment is a highly attractive one, with recent clinical success and opportunity fuelling significant transaction values - even for preclinical assets.

#### Recent immunotherapy deals for preclinical/ discovery products

Target	Acquirer	Deal value	Category	Stage (on deal signing)	Date announced	Additional
Blueprint Medicines	Roche	\$45m upfront, \$1bn total value	Kinases	Discovery	March 2016	Worldwide collaboration - to develop five lead candidates
Innate Pharma	Sanofi	\$436m total	NK bispecific	Discovery	January 2016	Research collaboration - antibodies to engage NK cells
Flexus Biosciences	Bristol-Myers Squibb	\$800m upfront, \$1.25bn total	IDO inhibitor (small molecule)	Preclinical	February 2015	Acquisition (Anti-T-cell suppressor technology)
Aduro Biotech	Novartis	\$200m upfront, \$50m equity investments, potential \$500m milestones	STING agonists (small molecule)	Preclinical	March 2015	Cyclic dinucleotides activate innate and adaptive immune responses
Collectis	Pfizer	\$80m upfront, \$265m total (plus 10% equity stake)	CAR -T	Preclinical	June 2014	Strategic alliance
Five Prime	Bristol-Myers Squibb	\$350m upfront, \$1.7bn total	Anti-CSF1R antibody	Phase 1	October 2015	License and collaboration agreement
Argenx	Abbvie	\$40m upfront, \$685m total value	GARP/ TGF-b	Preclinical	April 2016	Research collaboration on ARGX-115 and other future leads
Jounce Therapeutics	Celgene	\$225m upfront, \$2.6bn total value	ICOS antibody	Preclinical	July 2016	Strategic collaboration - including lead JTX-2011 and range of novel immunotherapies

Source: Company websites

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