

CIRCADIAN TECHNOLOGIES
LIMITED
(ASX.CIR, OTCQX.CKDX)
MAY 2012

Robert Klupacs, CEO & Managing Director



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WHO WE ARE

An emerging clinical stage company developing human therapeutic and diagnostic products from our extensive intellectual property assets in respect of VEGF-C, VEGF-D and VEGFR-3 and key relationships with leading cancer and eye research organisations.

REASONS TO INVEST

- **Clinical Stage Assets**
- **Increasing Diagnostics Portfolio generating revenues**
- **A platform with major deal/partnering potential across a range of products over next 3-18 months**
- **Investments coming up to major re-rating events**
- **Capability to get to key value adding events**
- **Experienced and talented management & advisors**

OUR PRODUCTS

- **Developing antibody therapies to treat cancer and eye disease**
 - » Based on unique ability to starve blood vessel and lymphatic vessel growth
 - » Targeting significant unmet clinical needs in oncology & ophthalmology
 - » Multi-billion dollar market opportunity
- **2 molecules currently in USA Phase 1 in cancer patients**
 - » VGX-100: Phase 2 to commence H1 2013 in brain cancer patients
 - » IMC-3C5: Being developed by Eli Lilly under licence
- **Clinical Trials in Eye diseases expected to commence H1**
 - » VGX-100 in combination with Lucentis for AMD
 - » VGX-100 in corneal disease such as Dry Eye
- **New generation cancer diagnostic developed in collaboration with Healthscope**
 - » Launch expected early Q3 2012

OUR PRODUCTS ARE DESIGNED TO IMPROVE ON EXISTING ANTI-ANGIOGENIC THERAPIES WHICH TARGET VEGF-A

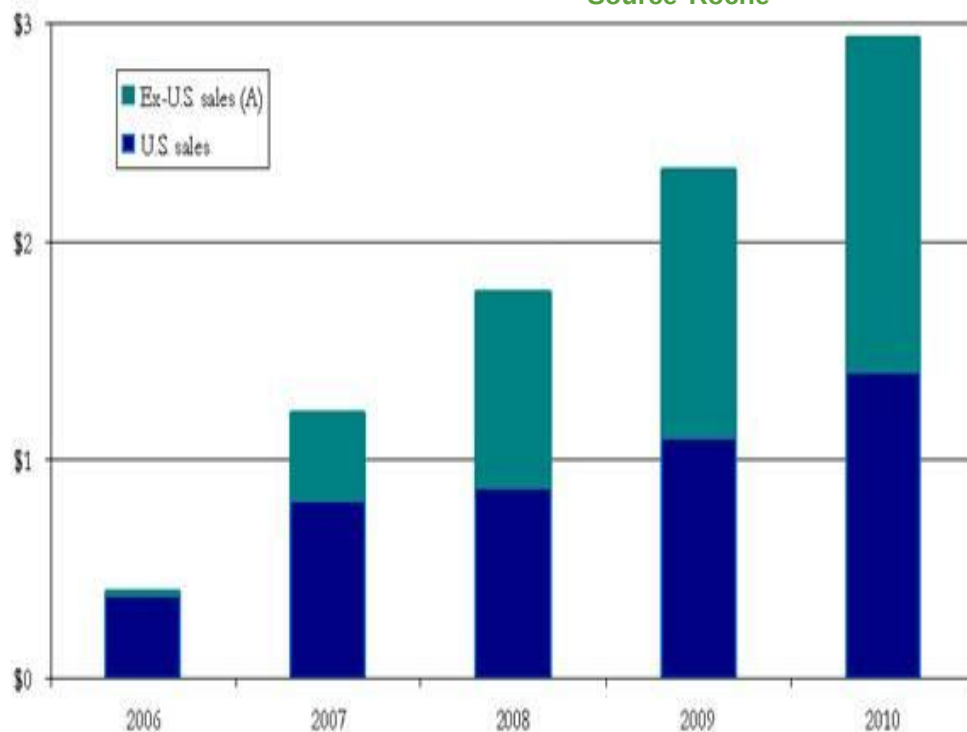


Avastin 2011 sales \$US5.8B (cancer)

Source Roche

Lucentis 2011 sales \$US2.9B (wet AMD)

Source Roche



IMPROVING ANTI-ANGIOGENESIS

A MAJOR COMMERCIAL OPPORTUNITY

- Avastin® (a humanised VEGF-A Antibody):
- Effective but not in all patients
 - Not all patients respond to therapy (30-50% response rate)
 - 25-50% of responders become “resistant” within 12 to 18 months
 - Potential reasons:
 - Tumour growth due to factors other than VEGF-A; and/or
 - Other angiogenic factors being turned on when VEGF-A blocked
(i.e. VEGF-C, VEGF-D)
 - Acts only to “starve” tumours but does not target metastatic spread

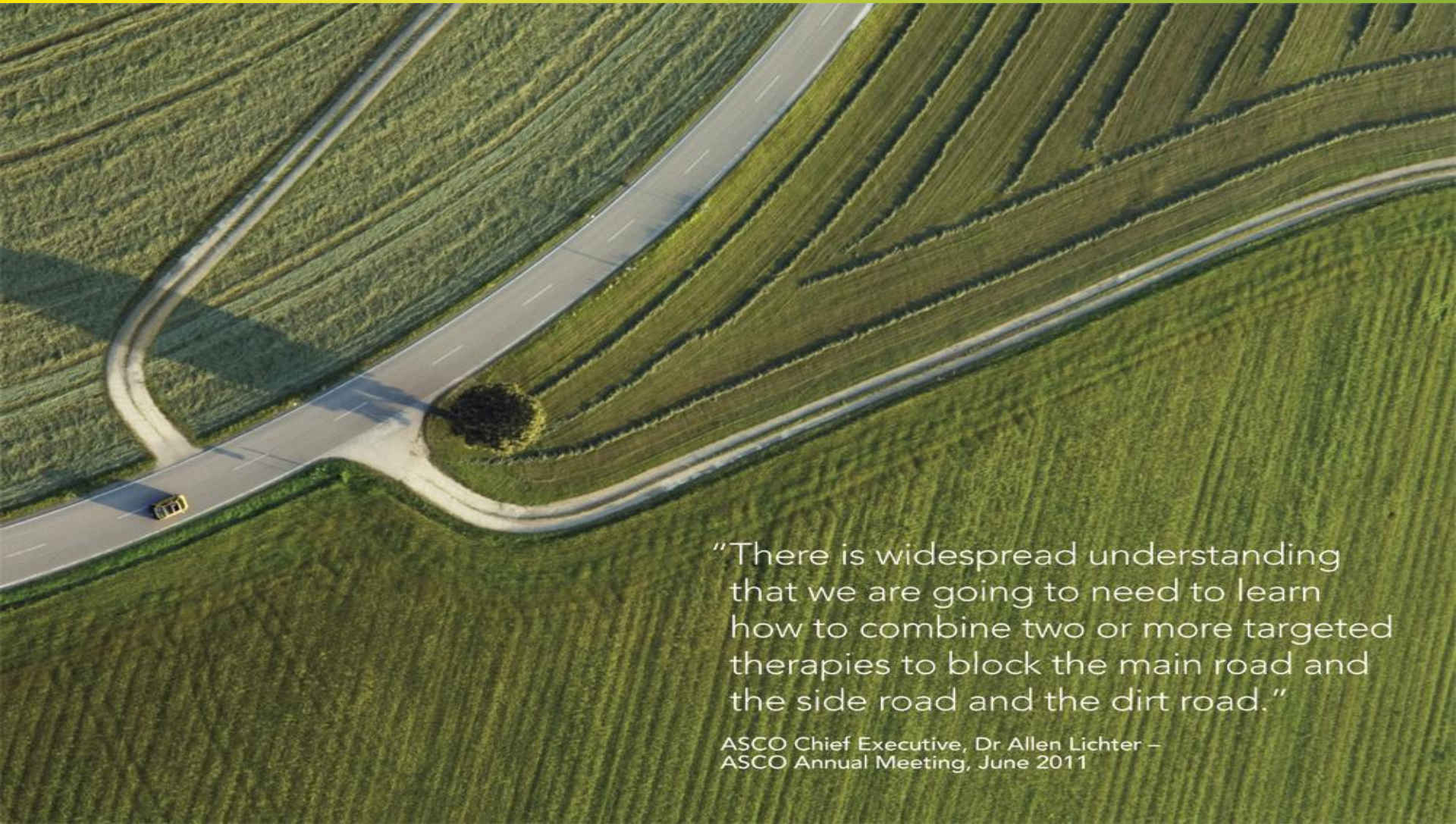
IMPROVING ANTI-ANGIOGENESIS A MAJOR COMMERCIAL OPPORTUNITY

- Lucentis® (a humanised VEGF-A Antibody):
- Approved for use in “wet” AMD (new blood vessel growth in retina causing leakage)
- Huge and Growing market due to aging
- Effective but not in all patients
 - Not all patients respond to therapy (50-70% response rate)
 - Potential reasons:
 - Blood vessel growth due to factors other than VEGF-A; and/or
 - Other angiogenic factors being turned on when VEGF-A blocked
(i.e. VEGF-C, VEGF-D)
 - Possible role of lymphatics

OUR APPROACH

Combine an VEGF-C antibody (VGX-100) with a VEGF-A antibody (Avastin or Lucentis) (or small molecule drugs which also target VEGF-A) to improve and maintain inhibition of new blood and/or lymphatic vessel growth

COMBINATION THERAPY OF TARGETED AGENTS IS BECOMING THE NEW PARADIGM IN CANCER THERAPY



"There is widespread understanding that we are going to need to learn how to combine two or more targeted therapies to block the main road and the side road and the dirt road."

ASCO Chief Executive, Dr Allen Lichter –
ASCO Annual Meeting, June 2011

ONCOLOGY

- **Initially targeting “niche” tumours then expanding into larger tumour types / markets after securing clinical proof**
- Glioblastoma (“Brain cancer”) – First Indication
- Ovarian cancers
- Pancreatic cancers
- Gastric cancers
- Colorectal cancers (“Bowel”)

GLIOBLASTOMA - A MAJOR UNMET CLINICAL NEED

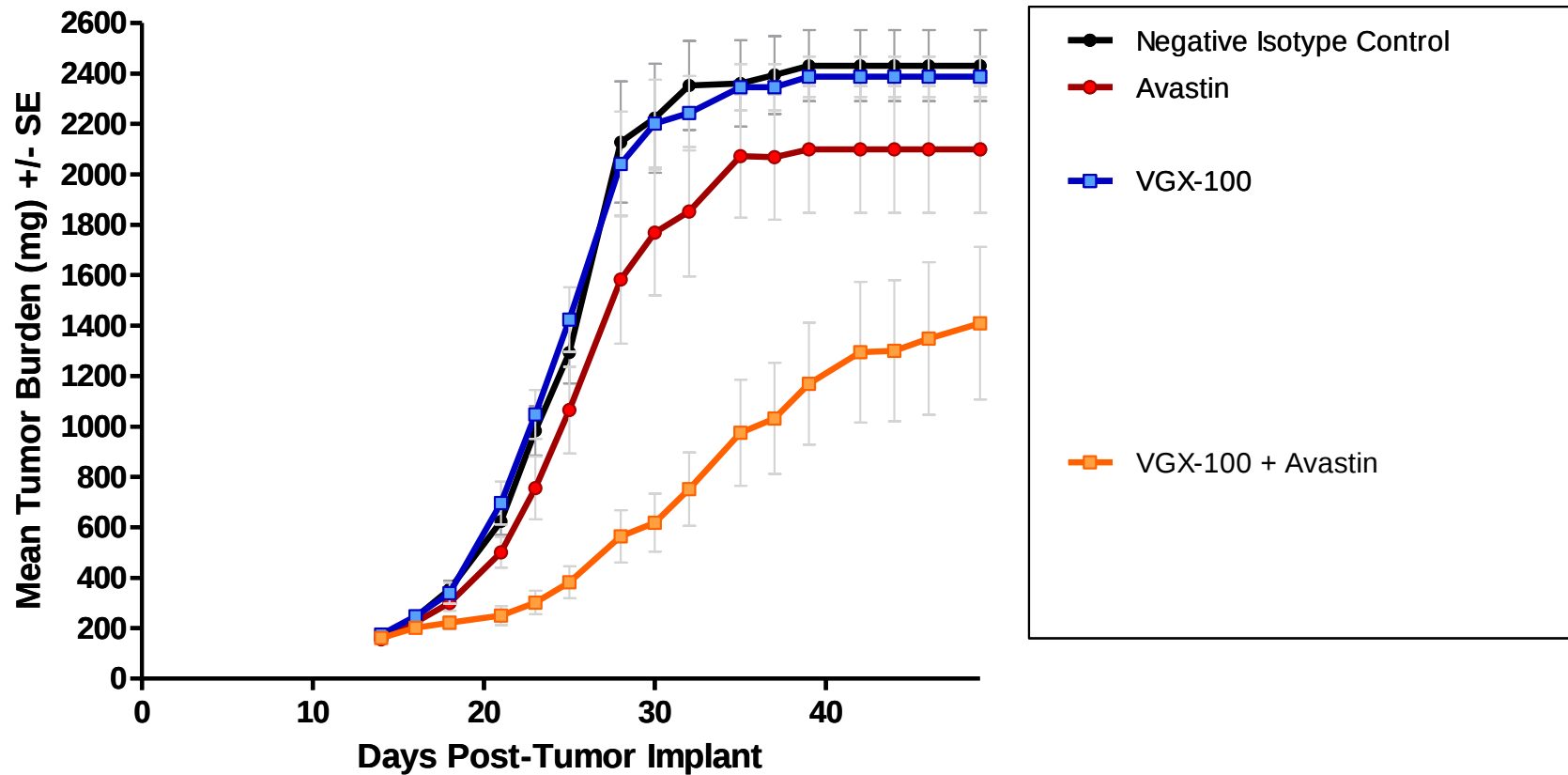
- In the US in 2010¹
 - Estimated diagnosed: 22,020
 - Estimated fatalities: 13,140
- The most aggressive malignant primary brain tumor in adults
- Nearly always fatal
- Possibility for fast track registration based on Phase 2b study.
- Phase 2b study aim to complete H1 '15.
- Fast track approval possible by H2 '15.
- Very strong interest from Key Opinion leaders worldwide

¹ Howlader N, Noone AM, Krapcho M, et al. *SEER Cancer Statistics Review, 1975-2008*, National Cancer Institute. seer.cancer.gov/csr/1975_2008/ based on November 2010 SEER data submission, posted to the SEER web site, 2011.

GLIOBLASTOMA - A MAJOR UNMET CLINICAL NEED WITH MAJOR COMMERCIAL POTENTIAL

- Expected Treatment Cost \$15-20,000 for 4 months therapy up to \$30,000 for 6 months treatment
- US patient pool initially up to 10,000 p.a, expanding to 50,000 ROW over subsequent years
- Initial market size \$300M p.a rising to \$1.5B p.a
- Avastin estimated to be generating \$300M p.a sales currently
- Possibility that VGX-100 could be approved and on the market by 2017/8
- Phase 2 studies combining VGX-100 and Avastin slated to start Q2 13 with initial results H2 14..

U87MG GLIOBLASTOMA TUMOR XENOGRAFTS: VGX-100 EFFECTIVE IN COMBINATION WITH AVASTIN



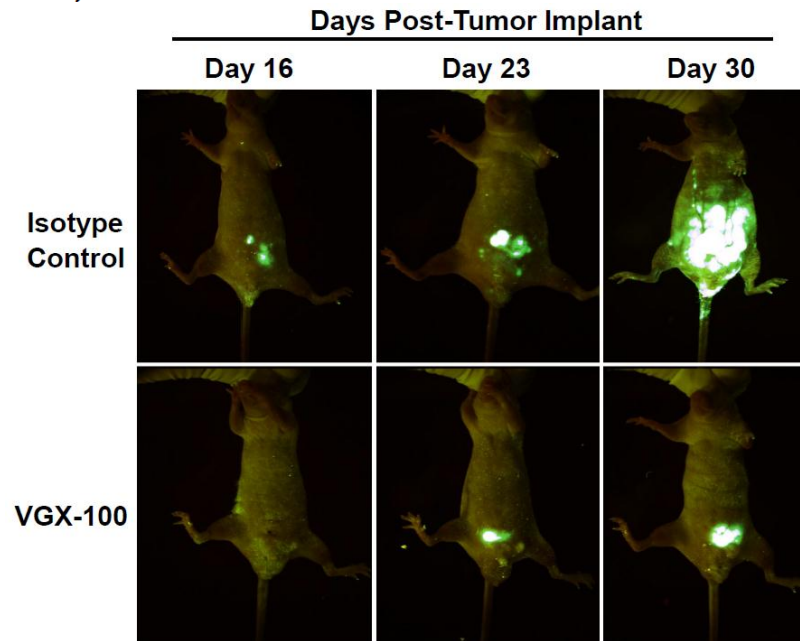
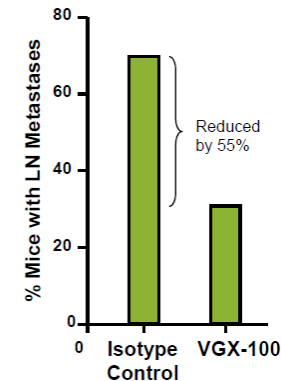
At Day 49, VGX-100 + Avastin reduces tumor burden by:

- 42% compared to control IgG
- 33% compared to single-agent Avastin.

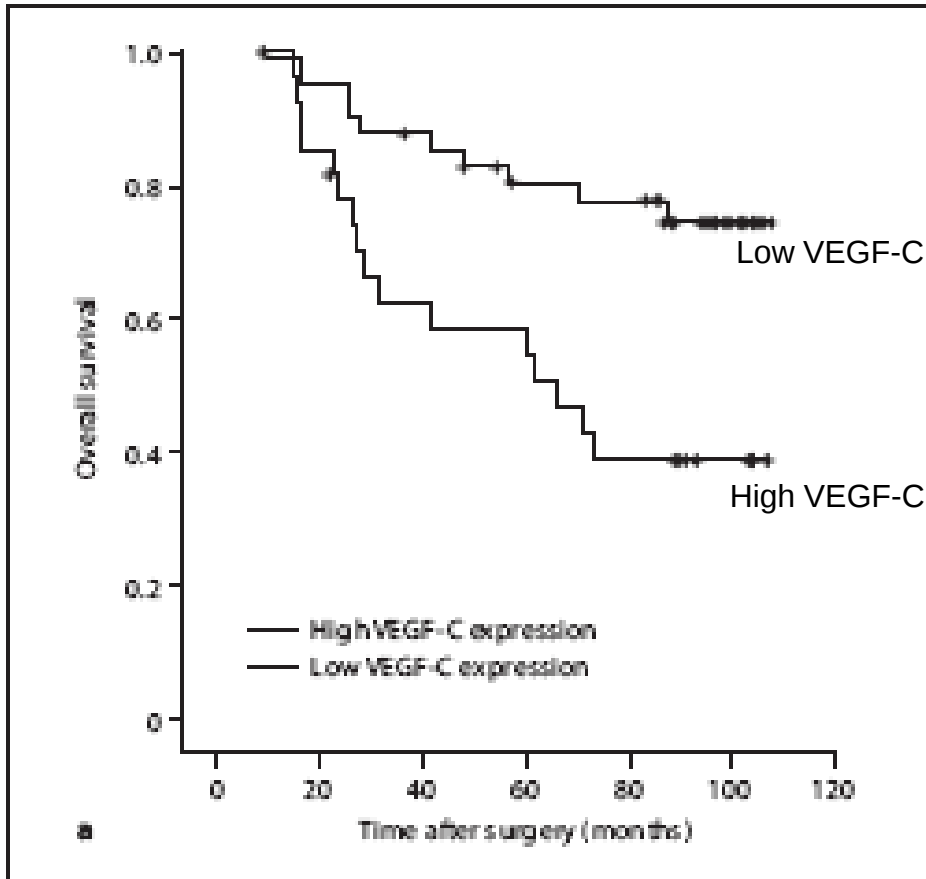
VGX-100 REDUCES METASTASIS IN AN ORTHOTOPIC PROSTATE CANCER MODEL

Group	# Mice	# Mice with LN Mets	% Mice with LN Mets	p value*
Isotype Antibody Control	17	12	71%	-
VGX-100	19	6	32%	0.019

* p value by Fisher exact test.



VEGF-C is a risk factor for colorectal cancer



69 CRC

VEGF-C correlated with:

- LN Metastases
- Clinical Stage

Elevated VEGF-C associated with:

- Decreased DFS
- Decreased OS

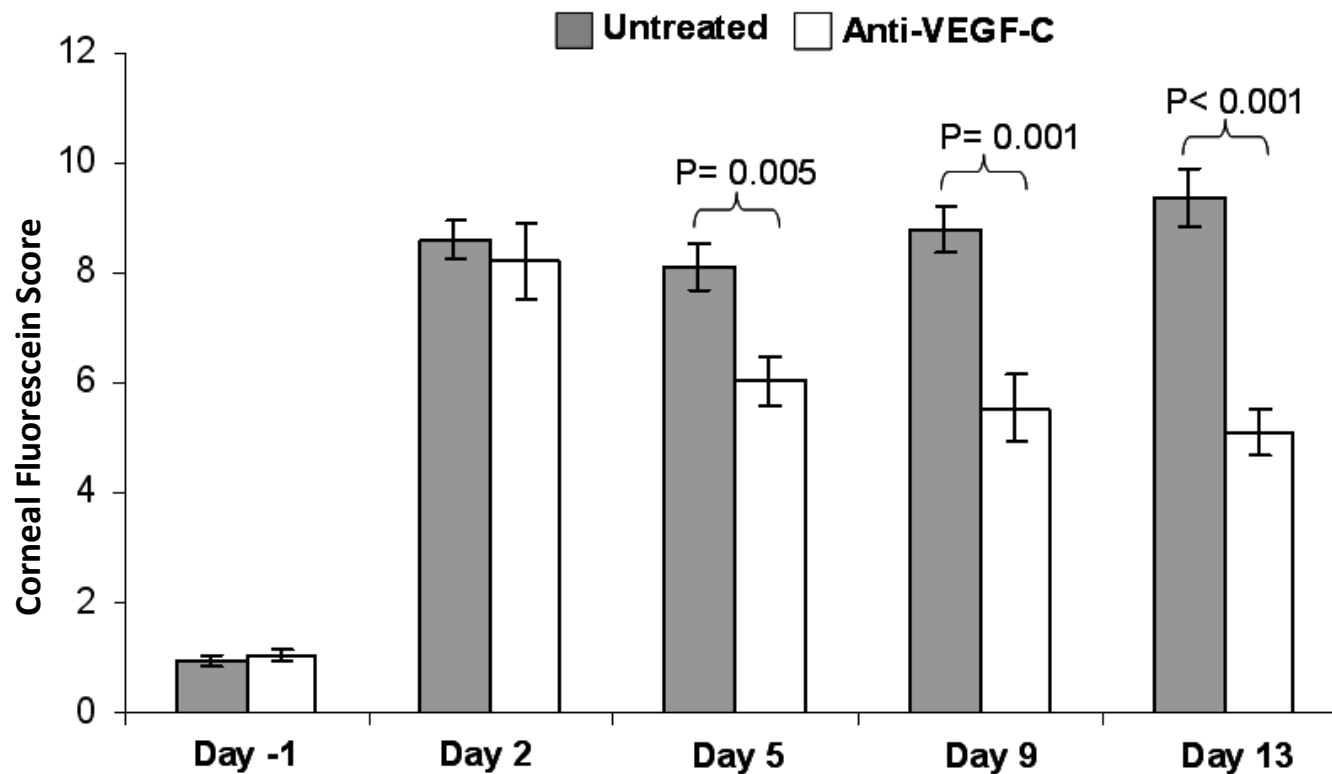
EYE DISEASE

- **Age related macular edema (AMD) – a major unmet clinical need with significant commercial potential**
- Currently in the USA 1.75 million individuals are affected
- 200,000 new cases are diagnosed each year.
- Lucentis \$3B sales in 2011
- Our market estimates based on “niche” non-responder market of 30-50% of all patients

DRY EYE DISEASE

- Multifactorial, immune-mediated disorder of the ocular surface affecting vision.
- Affects ~5M people aged >50yrs in USA.
- Adverse environmental conditions significant cause of DED.
- Limited therapeutic options. Usually artificial tears.
- Now known to be lymphatic mediated. Lucentis/Avastin ineffective.
- Currently, the only approved treatment is “Restasis” – 2011 sales >\$1B
- VGX-100 very effective in mouse model

VGX-100 REDUCES THE CLINICAL SIGNS OF DED



CANCERS OF UNKNOWN PRIMARY DIAGNOSTICS – A SOURCE OF NEAR TERM REVENUE

- » Development partnered with Healthscope
- » CUP 7th largest cancer fatalities
- » Healthscope (Aus,NZ, Singapore & Malaysia) Circadian retains ROW rights
- » Market launch in Aust, NZ expected June/July 2012
- » Market size in Healthscope territories up to 10,000 tests p.a
- » Pricing at \$>1000 Potential Royalty \$>1M p.a
- » Partnership discussions in US/Europe ongoing
- » Market in USA/Europe/Japan estimated to be 150,000 tests p.a

KEY FINANCIALS (CONSOLIDATED)

	30 June 11 \$000	31 Dec 2011 \$000
Cash	22,104	18,272
Listed investments (market value)	1,432	3,379
Net assets	21,824	
Revenue	1,850	
Operating expenses (incl. R&D, investment related exp's)	(12,893)	
Loss before tax	(11,043)	
Net cash outflows	(9,477)	
NTA per share	\$0.47	
Cash & listed assets per share	\$0.48	\$0.47
Share price	\$0.53	\$0.47

FINANCIALS – CASH FLOWS

- Current Cash - \$15.5m (Unaudited)
- Value of Listed Holdings - \$2.5M (Unaudited)
- Conservative Cash Burn 2011/12 and 2012/13 - \$9-12M p.a
- Well positioned to achieve key value adding milestones
- Does not take into consideration:
 - Increased R&D Tax Credit
 - Royalties on Sales of Diagnostics
 - Potential non-dilutive grant income (applications under review)
 - Further partnership income
 - Income from divestment of investments

FINANCIAL POSITION & SHAREHOLDER BASE

Top 10 shareholders: 52.8%

Investor	% of issued shares
HSBC Custody Nominees (Australia) Limited	18.88
Licentia Ltd	6.79
Ludwig Institute for Cancer Research	6.73
HSBC Custody Nominees (Australia) Limited GSCO ECA	4.57
Cogent Nominees Pty Limited	3.84
Capital Macquarie Pty Limited	2.97
Citicorp Nominees Pty Limited	2.61
Chemical Trustee Limited	2.50
National Nominees Limited	2.38
JFF Steven Pty Ltd	1.54
Total 10 shareholders own	52.8%
Total 20 shareholders own	60.1%

Financial Summary @ 15 May 2012 (unaudited)

Stock code:	CIR
Share price:	47.0c (AUD)
Shares issued:	46,396,928
Market cap:	~ A\$ 21.8 mill

Institutions/Funds: ~ 32%

Retail investors: ~ 40%

Professional investors: ~ 28%

KEY DEVELOPMENT MILESTONES

Activity	Timeline
CUP Test Launch	6-7/2012
VGX-100 Phase 1 Clinical Trial update	8/2012
VGX-100 Phase 1 studies completed	H2 2012
IMC-3C5 Phase 1 trials reported	H2 2013
Phase II studies in cancer patients start (Multiple Indications)	Q1 2013
VGX-100 IND Filing Eye Disease	H1 2013
VGX-100 Phase ½ Trials in Eye disease commence	H1 2013
Expansion of Diagnostics portfolio	H2 2012
Clinical proof-of-concept in first cancer indication	2H 2014
Clinical proof-of-concept in first eye disease indication	2H 2014
Partnering	Late H2 2012 +

AN INVESTMENT WITH SIGNIFICANT UPSIDE

Research Report from Edison Research March 14 2012

“....On a DCF basis to March 2012, Edison estimates a revised indicative value of A\$100m (A\$2.16 per share).

We expect value to develop strongly as the pipeline develops and as new VGX-100 indications become clearer...”

CIR current share price at May 15 is 47c

APPENDIX

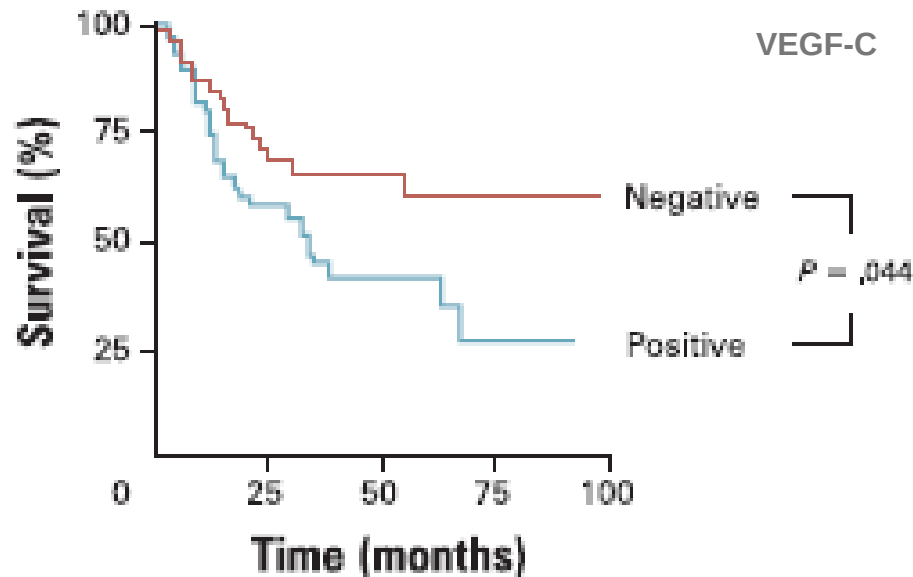
VEGF-C

A MAJOR TARGET FOR IMPROVED ANTI-CANCER AGENTS

- Can stimulate VEGFR-2 and VEGFR-3 mediated angiogenesis (inhibition leads to “tumour starvation”)
- Can stimulate VEGFR-3 mediated lymphangiogenesis, a major route of metastatic spread (inhibition slows spread with survival benefits)
- VEGF-C has also been shown to be a well recognised survival prognostic factor in a number of tumour types

Some examples

VEGF-C levels correlate with lymph node mets and decreased survival in gastric cancer



91 Gastric Adenocarcinomas

VEGF-C correlated with:

- LN metastases
- Decreased survival

VEGFR-3 is an independent prognostic markers

THERAPEUTIC FOCI

- Oncology – in combination with existing therapies
- Front of Eye Disease (Cornea) – mono-therapy (separate presentation)

THERAPEUTIC FOCUS

ONCOLOGY

- **IMC-3C5 (fully human VEGFR-3 ab)**

- *Being developed by Imclone*

- *Phase 1 commenced April 2011*

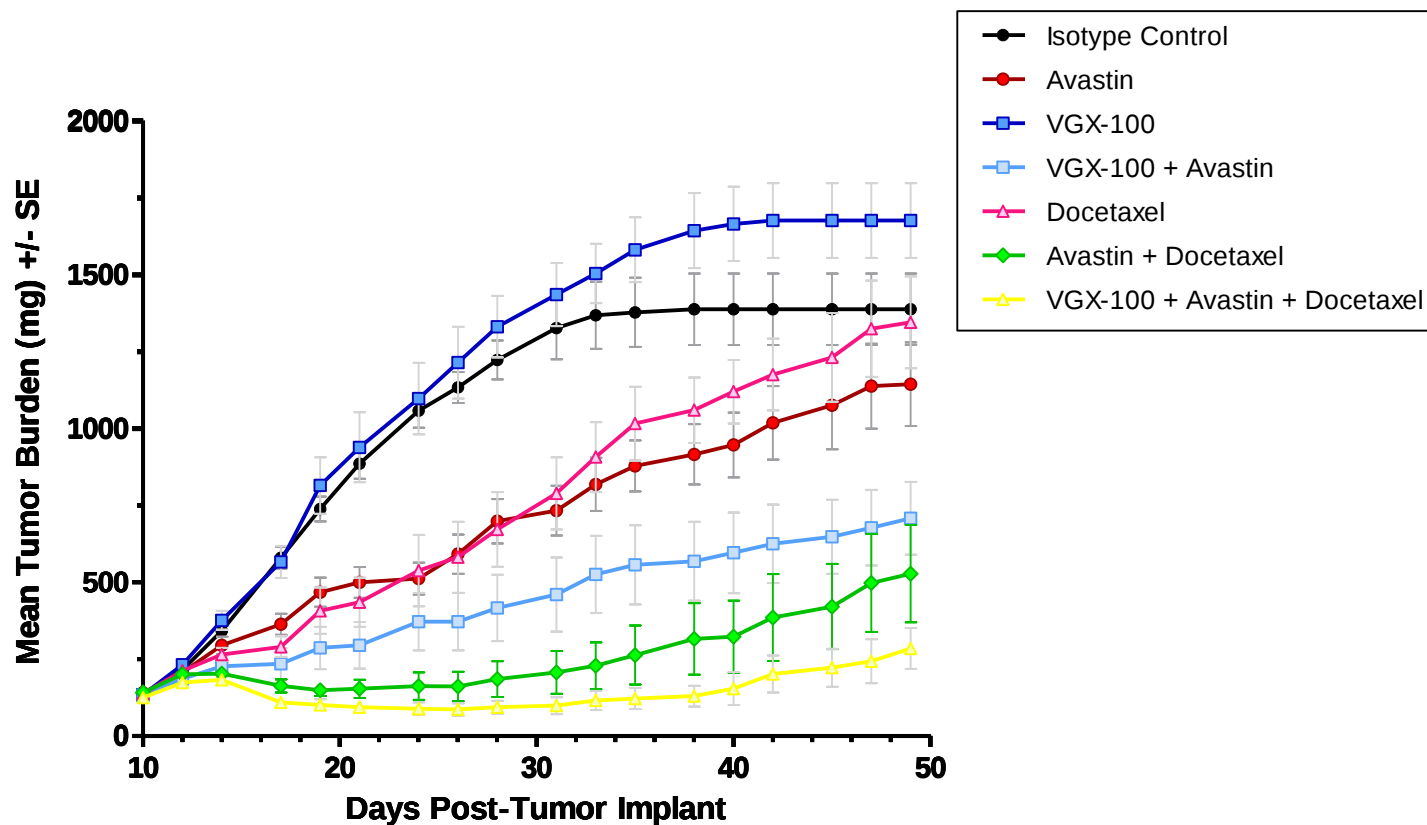
- **VGX-100 (fully human VEGF-C ab)**

- *In –house development*

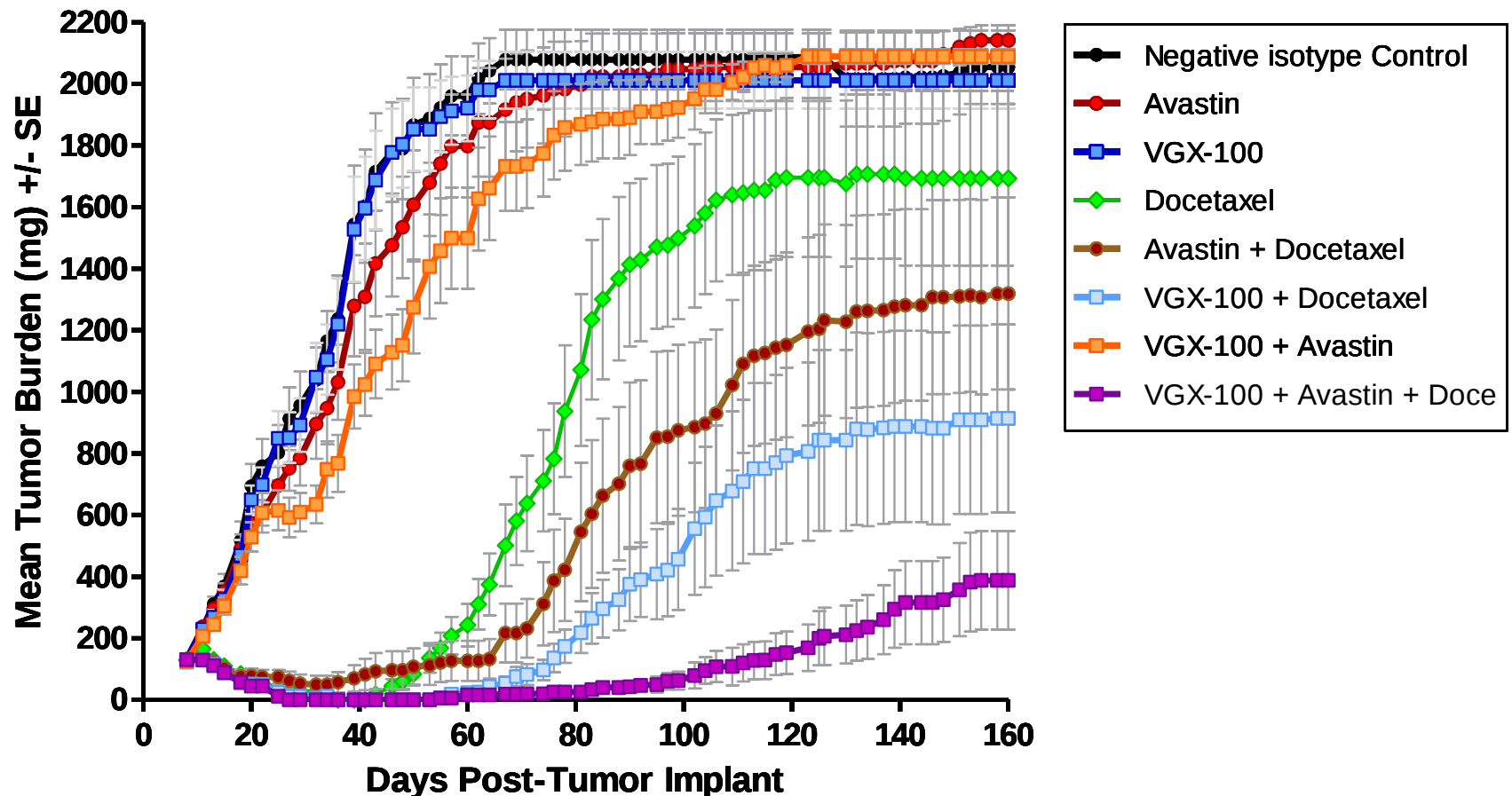
- *Phase 1 commenced in USA January 2012*

- *Lead indication -glioblastoma*

H292 NSCLC Tumor Xenografts: VGX-100 effective in combination with Avastin

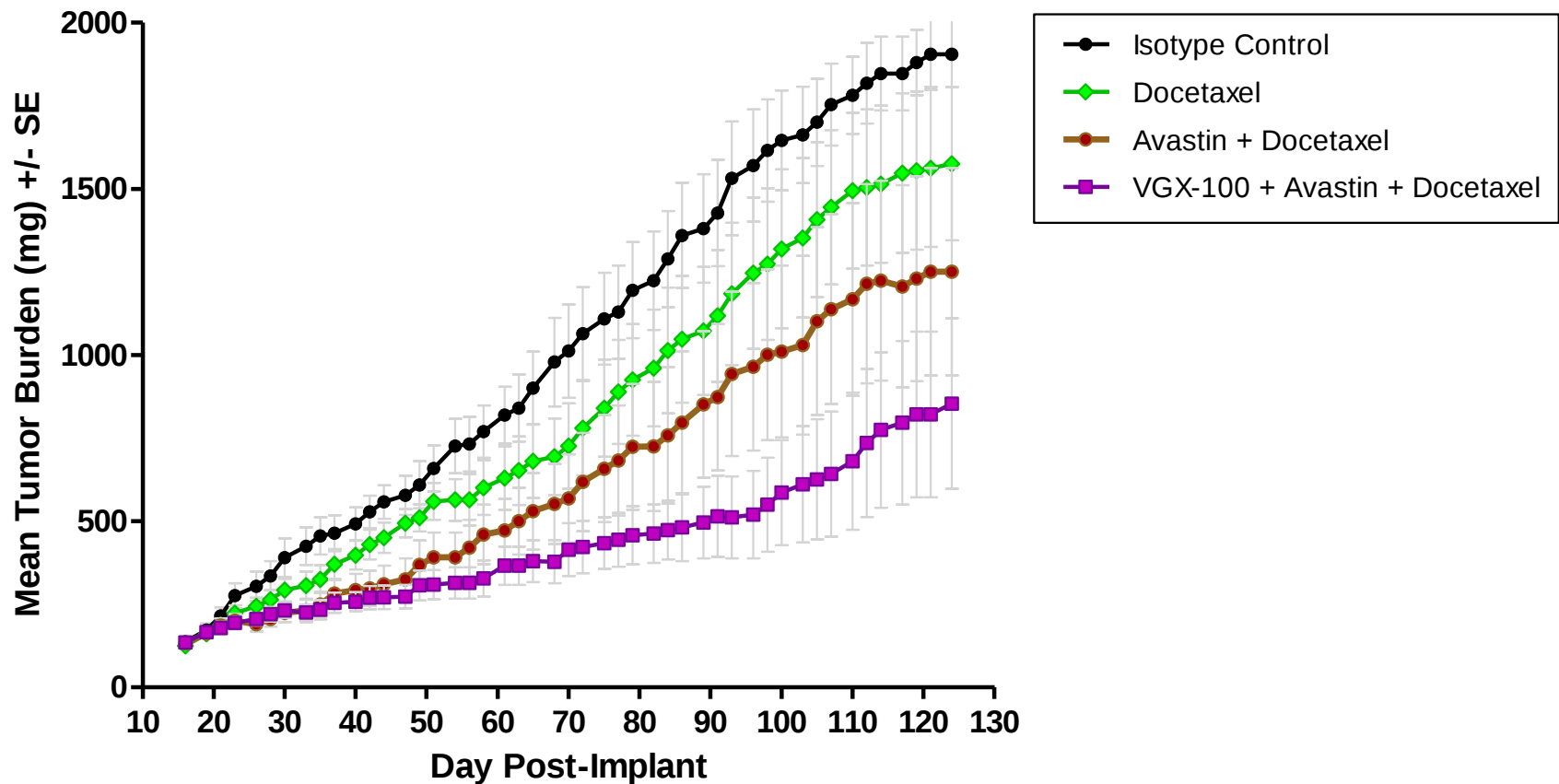


VGX-100 SINGLE-AGENT & COMBINATION THERAPY IN PC-3 PROSTATE CANCER XENOGRAFTS

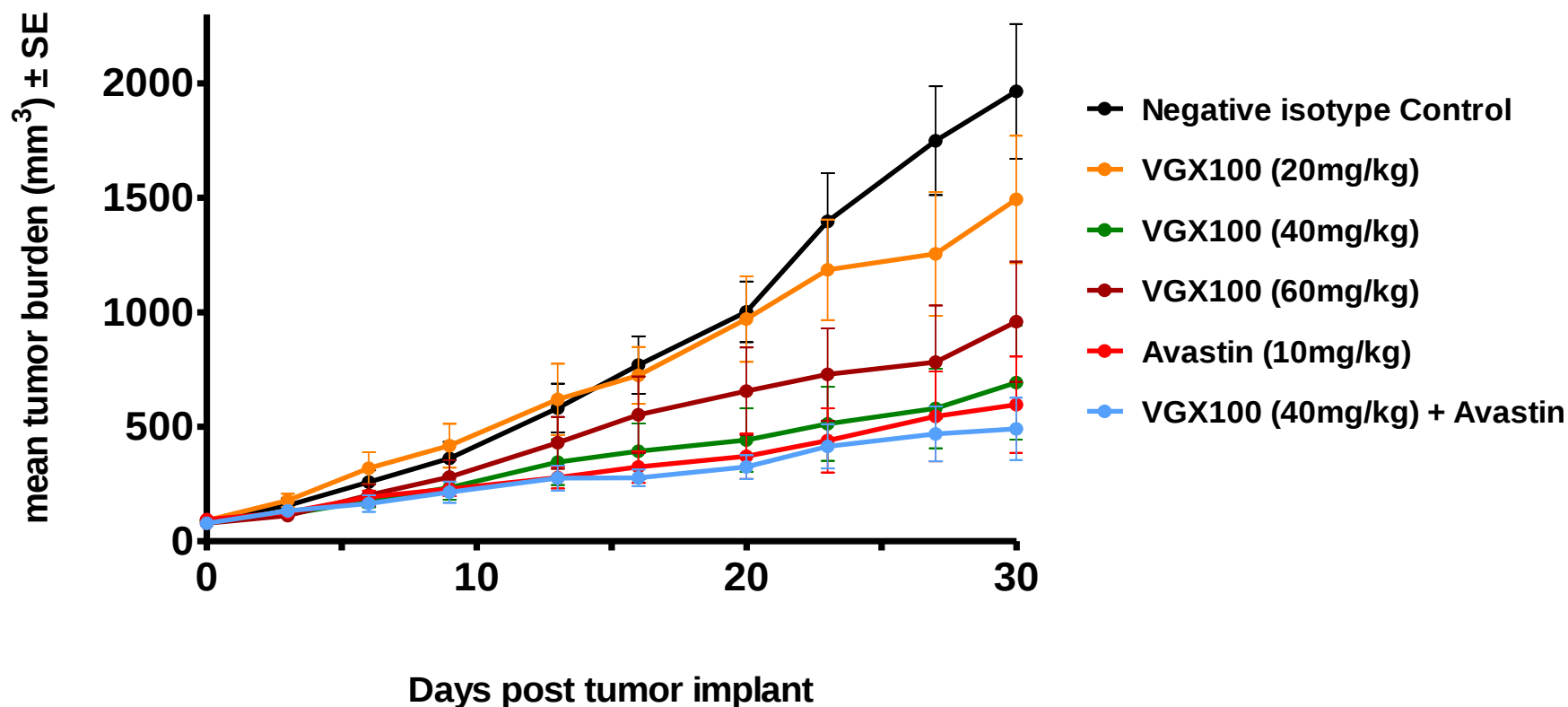


Docetaxel: Weekly IV at 10 mg/kg for 3 weeks. Vehicle: 10% EtOH, 10% Tween 20, 80% water.

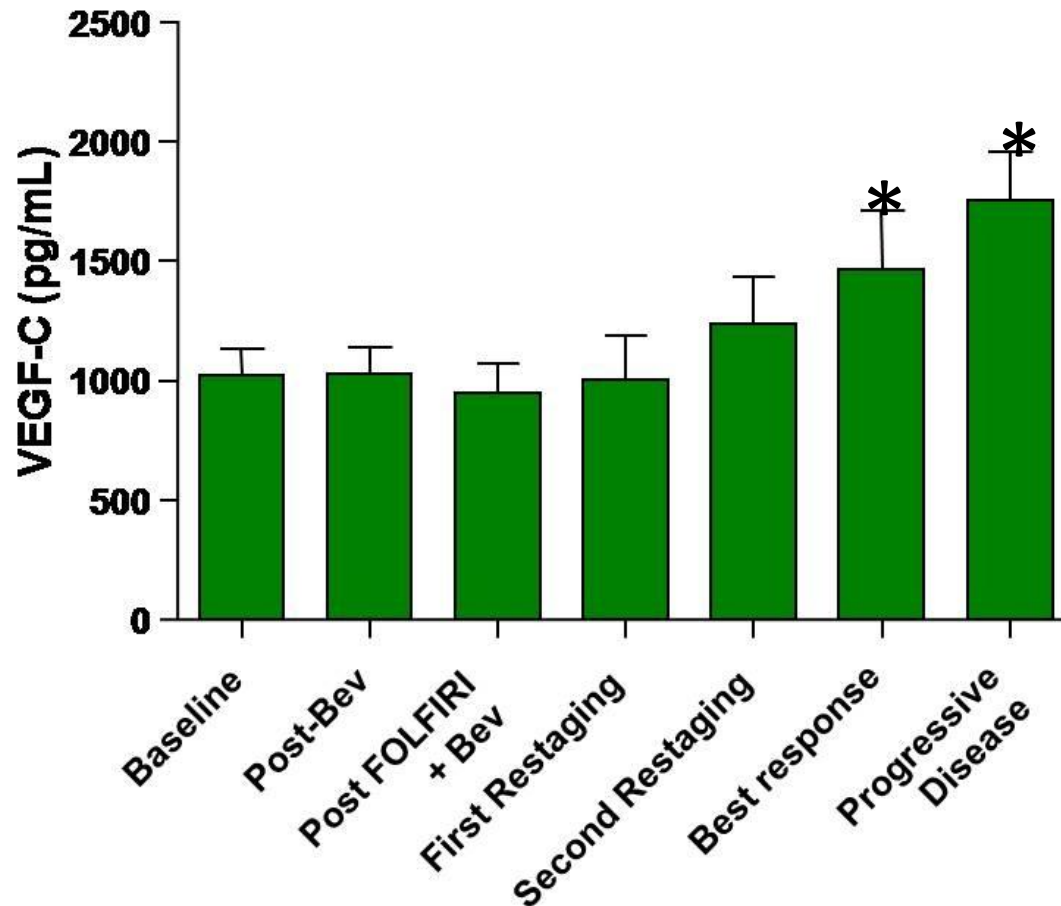
VGX-100 enhances Avastin + Docetaxel therapy in OVCAR-8 ovarian cancer tumours



VGX-100 is active as a monotherapy in KP4 human pancreatic tumour xenografts



HAVE NOW SHOWN THAT VEGF-C MAY BE A PREDICTIVE BIOMARKER FOR AVASTIN RESISTANCE



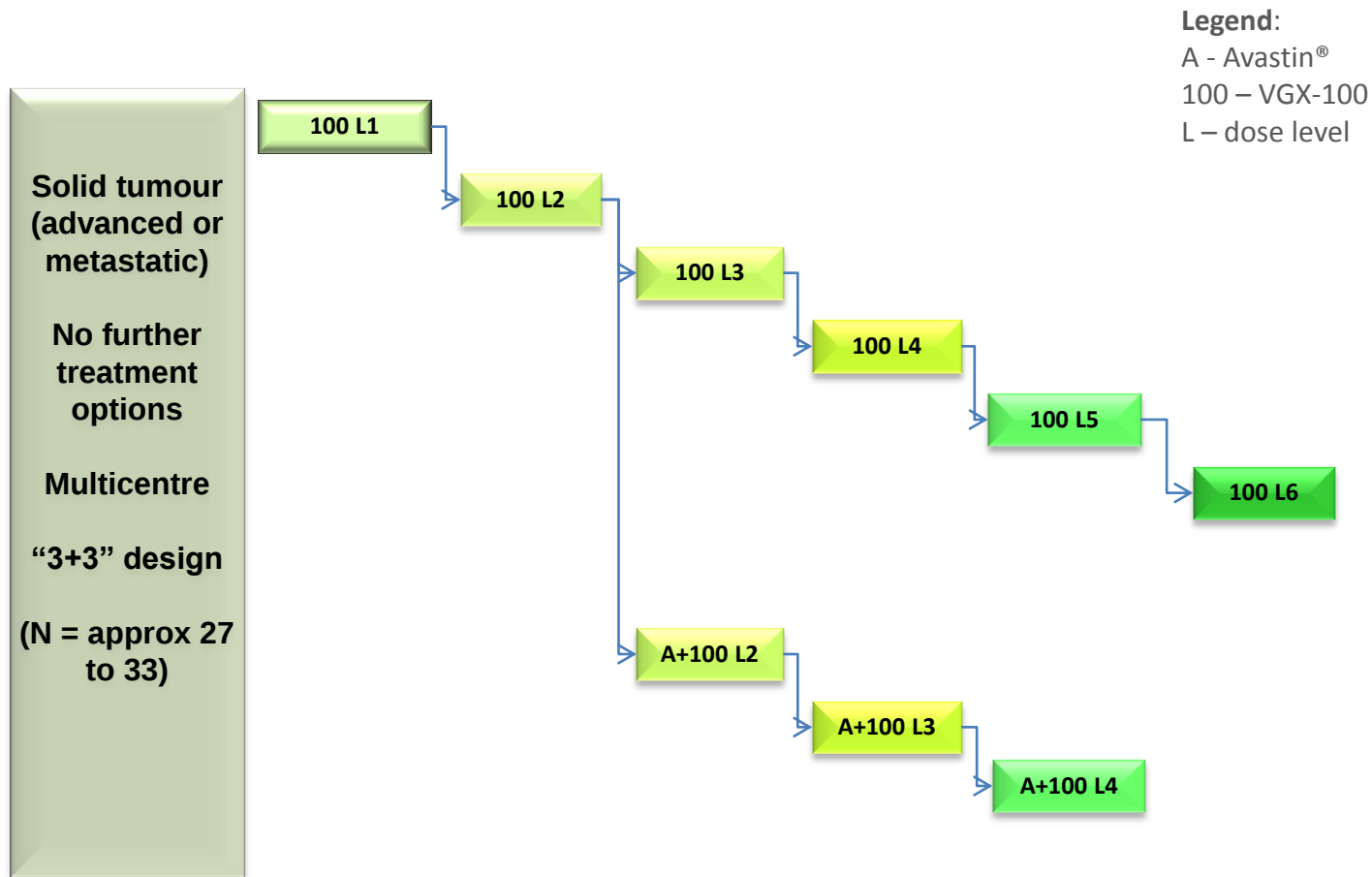
VEGF-C levels begin to rise
BEFORE tumours
Stop responding to Avastin.

Highlights major potential
for improving therapy by
combining VEGF-A and VEGF-C
blockade

VGX-100 TARGET PRODUCT PROFILE IN ONCOLOGY

- **Indication:**
 - Co-administered with anti-angiogenic agent eg (Sutent[®], Nexavar[®], Avastin[®]) and standard of care
 - Targeting glioblastoma and colorectal cancer as first indications
 - To develop through collaborations at least one of breast, lung, renal and/or potentially ovarian cancer in combination with anti-angiogenic agents most likely to be Avastin[®]

VGX-100 PHASE I FIRST-IN-HUMAN STUDY



TREMENDOUS & EXPERIENCED MANAGEMENT & ADVISORS

- Prof George Morstyn ex Amgen
- Dr Errol Malta ex Amgen
- Dr Ralph Smalling ex Amgen
- Dr Russell Howard ex Maxygen/NIH
- Dr Jonathan Skipper Ludwig Institute
- Mr Carlo Montagner ex Abraxis/Sanofi-Aventis
- Prof Kari Alitalo University of Helsinki
- Dr Megan Baldwin ex Genentech
- Mr Mark Sullivan ex GSK/Gilead

OVER 150 Drug Development Projects Combined

PARTNERING ANTIBODIES FOR CANCER THERAPY AT EARLY STAGE CAN BE VERY LUCRATIVE

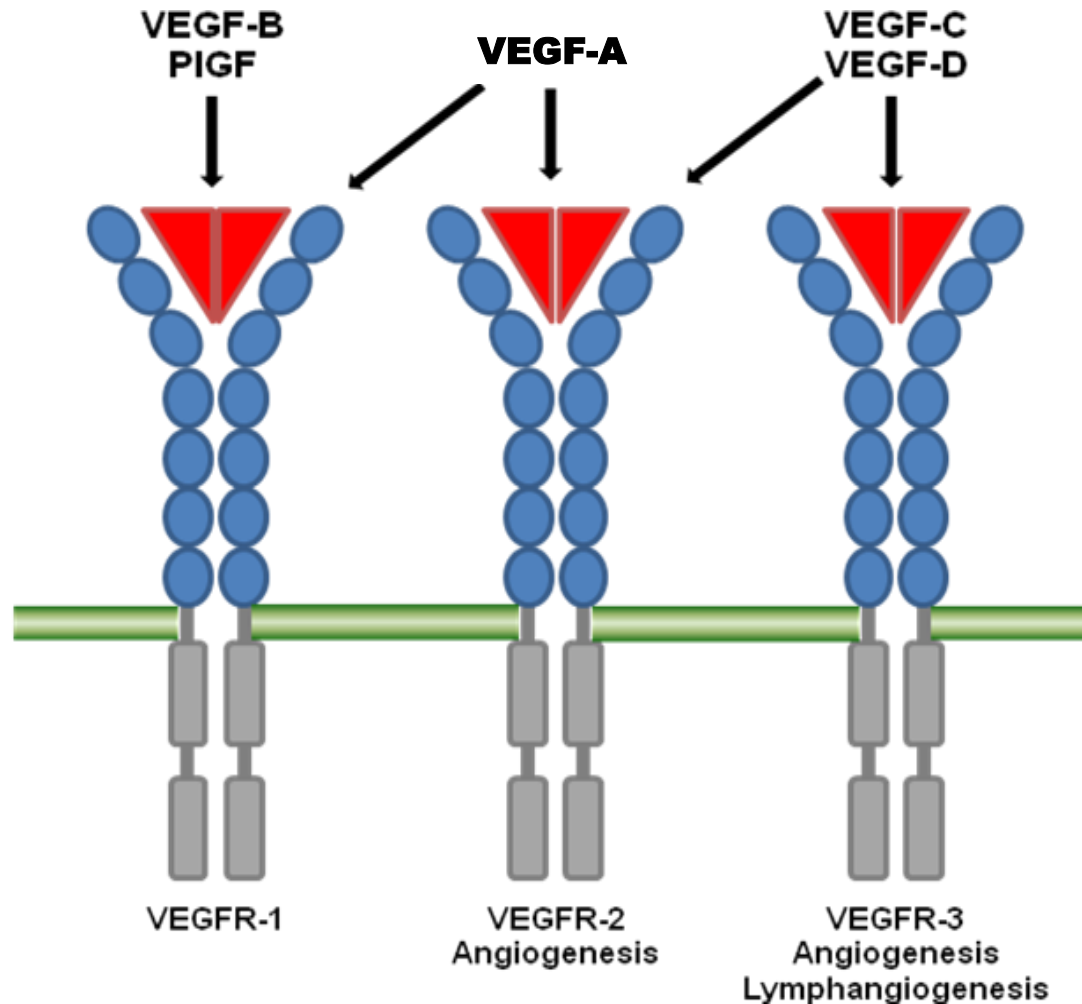
Parties	Date	Size	Technology
BiolInvent/Thrombogenics /Roche	Jun 08	\$US800M	Exclusive licence to PlGF (anti-angiogenic) Abs in oncology. \$US75M upfront. \$US700M milestones. Double digit royalties
Pierre Fabre/Abbott	Feb 10	\$US100M +	Exclusive licence to pre-clinical c-met antibody. \$US25M up-front. Other terms confidential
Merrimack/Sanofi	Nov 09	\$US530M	Exclusive licence to MM-121-HER-3 ab in early Phase 1. \$US60M up-front. \$470M milestones. US co-promotion
Abbott/LICR	Nov 08	\$US150-200M	Exclusive licence to 2 nd generation EGFR Ab in oncology which has completed 8 person Phase 1 study
Dyax/Sanofi-Aventis	Feb 08	\$US500M	Exclusive licence to Tie-1 Ab DX-2240 and phage display in selected applications
GSK/OncoMed	Dec 07	\$US1.4B	Exclusive licence/co-development of 4 selected stem cell Abs in cancer

COMPETITIVE LANDSCAPE

BIOLOGICAL ANTI-ANGIOGENIC AGENTS

Company	Molecule	Target	Partner & Partnering Stage	Clinical Stage	Indication	Relevance To CIR
Regeneron	Aflibercept (VEGF Trap)	VEGF-A PIGF	Sanofi Phase 1	P3	1 st and 2 nd line CRC 2 nd line NSCLC 1 st line hormone resistant prostate cancer	Positioned as direct competitor to Avastin, NOT as complementary agent
Regeneron	Aflibercept	VEGF-A PIGF	Bayer Phase1	P3	Wet AMD	CIR agents not for “back of eye” disease
Imclone	IMC-1121b	VEGFR-2	Eli Lilly Phase 1	P3	Breast, HCC	Positioned as direct competitor to Avastin, NOT as complementary agent
Pfizer	CVX-060	Ang-2	N/A	P2	Glioblastoma	Target outside VEGF pathway
Bioinvent	TB-403	PIGF	Roche Pre-clinical	P2	Glioblastoma	Being combined with Avastin
AVEO	AV-299	HGF	Merck (terminated) Pre-clinical	P2	Glioblastoma	Target outside VEGF
Tracon	TRC-105	Endoglin	None	P1	Ovarian	Target outside VEGF
Genentech	MNRP-1685	Neuropilin-1	None	P1	Solid Tumours	Likely to be combined with Avastin
Genentech	MEGF-0444	EGFFL7	None	P1	Solid Tumours	Likely to be combined with Avastin

OUR IP COVERS MAJOR COMPONENTS OF VEGF PATHWAY



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