BIOTECH SHOWCASE
PARC 55
SAN FRANCISCO
9 JANUARY 2013

Robert Klupacs, CEO & Managing Director

Circadian Technologies (ASX.CIR, OTCQX.CKDXY)

circadian

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CORPORATE SNAP SHOT

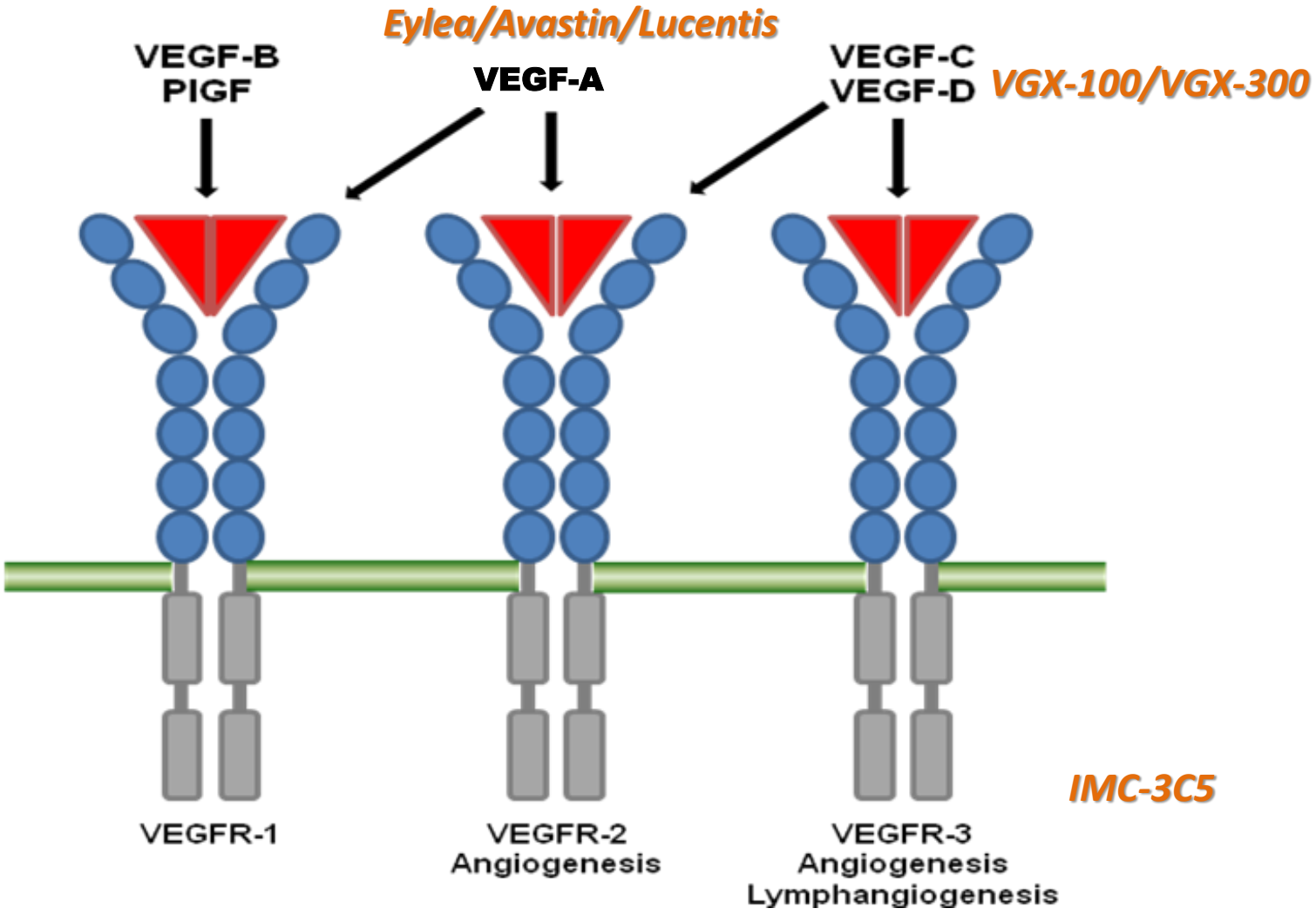
- Australian based emerging clinical stage company listed on ASX and OTCQx
  - 12 FTE's plus extensive range of CRO's, CMO's and consultants
- Developing human therapeutic and diagnostic products in oncology and eye disease
- Extensive and worldwide dominant intellectual property platform in respect of VEGF-C, VEGF-D and VEGFR-3
  - key mediators of angiogenesis and lymphangiogenesis
- Strategic relationships with leading cancer and eye research organisations worldwide

OUR PRODUCTS

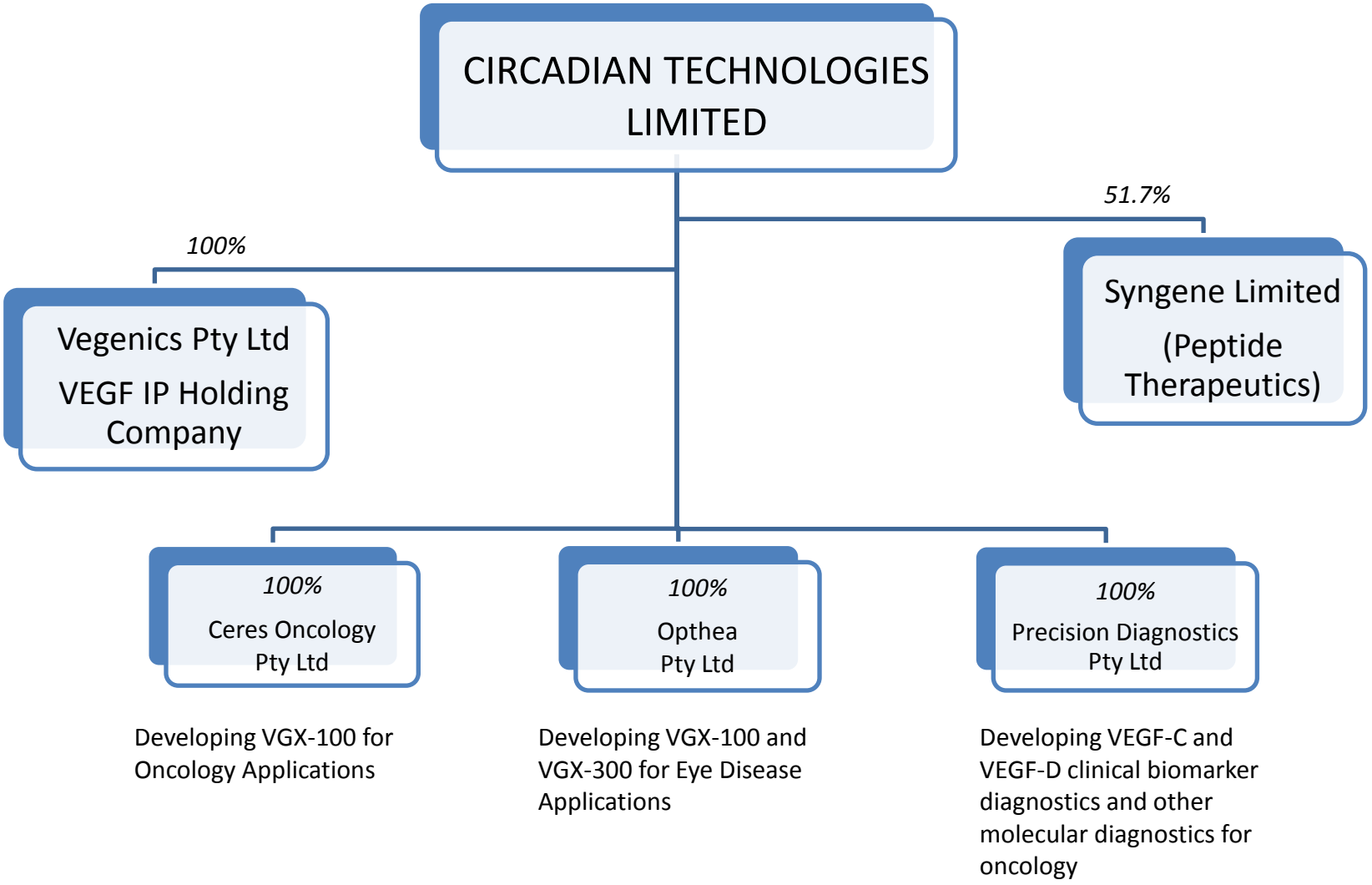
- **Developing antibody therapies to treat cancer and eye disease**
  - » Based on unique ability to starve blood vessel and lymphatic vessel growth
  - » Targeting significant unmet clinical needs in oncology & ophthalmology
  - » Multi-billion dollar market opportunity
- **2 molecules currently in USA Phase 1 in cancer patients**
  - » VGX-100: Phase 2 start H2 2013 in lymphedema & H1 2014 in rGBM patients
  - » IMC-3C5: Being developed by Eli Lilly under licence
- **Clinical Trials in Eye diseases expected to commence H2 2014**
  - » VGX-100 or VGX-300 in combination with Lucentis/Eylea for wet AMD
  - » VGX-100 or VGX-300 in corneal disease such as Dry Eye
- **New generation cancer diagnostic developed in collaboration with Healthscope**
  - » Launched in Asia Oct 2012

THE VEGF PATHWAY IS NOT JUST VEGF-A

OUR IP COVERS OTHER MAJOR MOLECULES



OUR CORPORATE STRUCTURE



FINANCIAL POSITION & SHAREHOLDER BASE

Top 10 shareholders: 54.4%

Investor	% of issued shares
BNP Paribas Noms Pty Ltd	17.10
Citicorp Nominees Pty Ltd	8.78
Ludwig Institute for Cancer Research	6.43
HSBC Custody Nominees (Australia) Limited GSCO ECA	5.33
National Nominees Limited	4.73
BNP Paribas Noms Pty Ltd	3.67
Capital Macquarie Pty Limited	2.84
Chemical Trustee Limited	2.39
4 Eyes Limited	1.67
JFF Steven Pty Ltd	1.47
Total 10 shareholders own	**54.4%**
Total 20 shareholders own	**61.9%**

Financial Summary @ 4 January 2013 (unaudited)

Stock code:	**CIR**
Share price:	**35.5c** (AUD)
Shares issued:	48,481,642
Market cap:	~ A$**17.5** mill
Cash holdings: Listed investments: (ASX: ANP, OIL)	~ A$**11.8** mill A$**1.8**mill

Institutions/Funds: ~ 35%

Retail investors: ~ 37%

Professional investors: ~ 28%

FINANCIALS – CASH FLOWS

- Current Cash - $A11.5m (Unaudited) excluding Syngene
- Value of Listed Holdings - $1.8M (Unaudited)
- Predicted Cash Burn 2012/13 and 2013/14- $6.0 -8.0M 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
  - Further partnership income
  - Income from divestment of investments

THERAPEUTIC & DIAGNOSTICS DEVELOPMENT

3 specific 100% owned subsidiaries

Ceres Oncology Pty Ltd (Oncology Therapeutics)

Precision Diagnostics Pty Ltd (Clinical Diagnostics)

Opthea Pty Ltd (Eye Disease Therapeutics)


CERES
ONCOLOGY

Executive Summary

Anti-angiogenic therapies: $30B market (2011)

- Proven efficacy
- Limited by escape and relapse

VGX-100: new treatment to block VEGF-C

- Targets both blood and lymph vessel growth
  - Blocks a treatment escape route for Avastin® (anti-VEGF-A)
  - Enhances existing therapies
- Fully human, monoclonal antibody

Target Indications

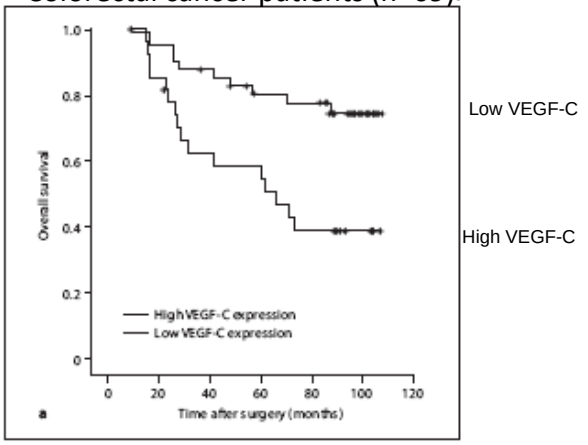
- Monotherapy in lymphedema
  - Significant unmet need
  - Rapid development
- Combination with standard of care in oncology, including
  - Glioblastoma multiforme
  - Ovarian
  - Colorectal cancer

CERES ONCOLOGY

Elevated VEGF-C implicated in poor outcomes

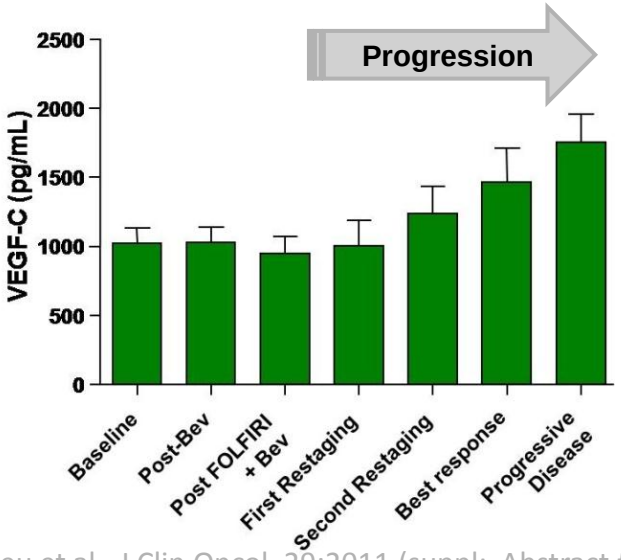
- Reduced survival
  - Gastric, lung, colorectal, lung, breast, pancreatic, ovarian cancers
- Increases vascular density
  - melanoma, breast, pancreatic, colorectal, lung

Colorectal cancer patients (n=69)



Hu et al., Eur Surg Res, 39: 229-238, 2007.

- Escape from Avastin®
  - Non clinical data
    - Glioblastoma multiforme
  - Clinical data:
    - VEGF-C increases at the time of Avastin® + FOLFIRI progression in colorectal cancer (n=40)

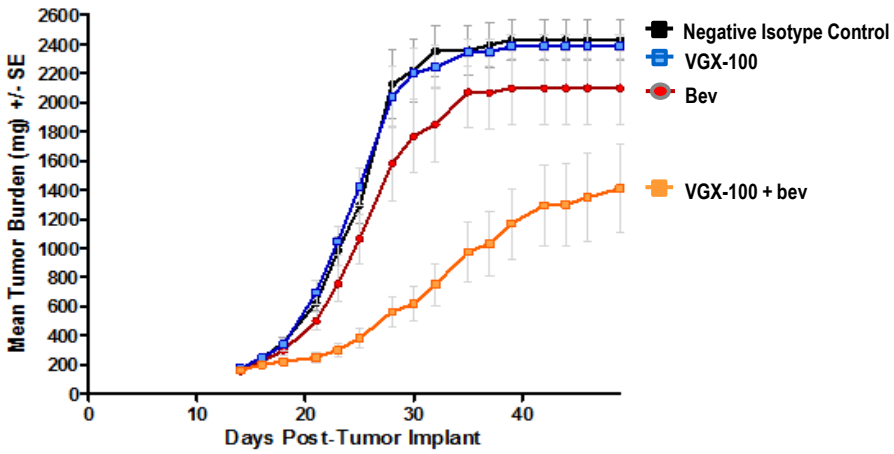


C.Lieu et al., J.Clin.Oncol. 29:2011 (suppl; Abstract #3533).

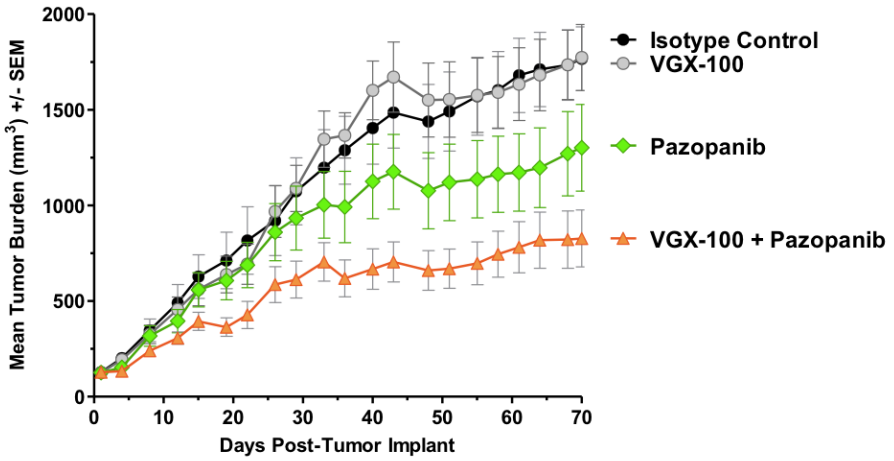
CERES ONCOLOGY

VGX-100 is effective in murine models of cancer: Alone or in combination with anti-angiogenic agents

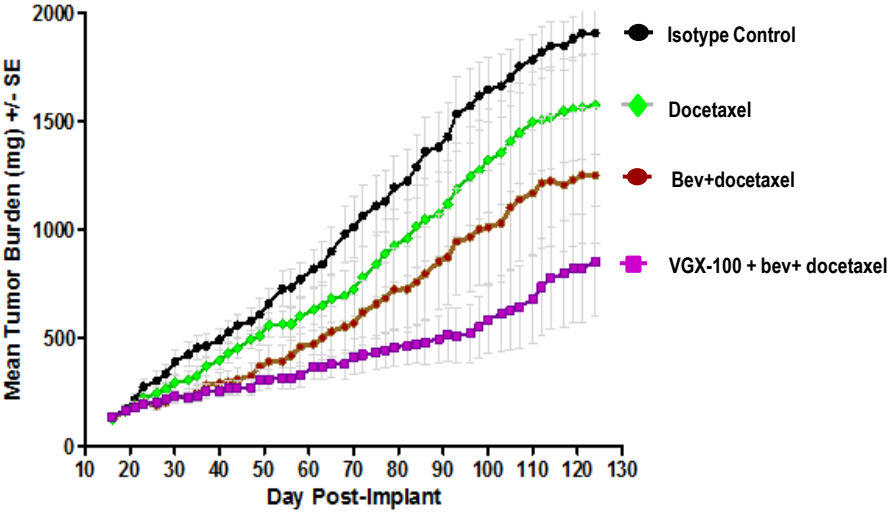
U87MG Glioblastoma



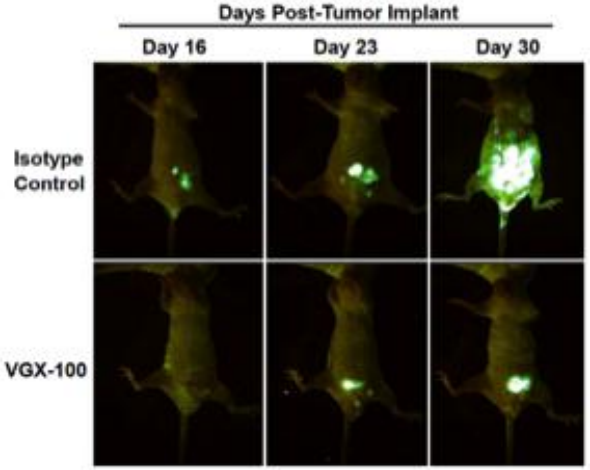
Colo205 Colorectal



OVCAR-8 Ovarian Cancer



Metastatic PC3 prostate cancer model



Multiple Indications with important advantages

	Lymphedema	Recurrent Glioblastoma multiforme	Recurrent Ovarian	Metastatic colorectal cancer
Rationale	++	+++	++	+++
Feasibility	+++	++	+++	++
Opportunity	++ (10-40% of breast cancer survivors)	++ (n=22,910 new cases in 2012)	+ (n=22,280 new cases in 2012)	+++ (n=149,600 new cases in 2012)
Lowest Regulatory Hurdle	+++ (likely Orphan)	++	+	+
Speed to proof of concept	+++	++	+++	++
Speed to approval	+++	++	++	+

CERES ONCOLOGY

Lymphedema is an important unmet medical need

Rationale

↑VEGF-C in lymphedema

Significant increase in case matched control study.

Miller et al. J Clin Oncol 27:15s, 2009 (suppl; abstr 9523)

Interstitial hypothesis

Batse DO Pathophysiology (2010) 17(4): 289-94

TKI (pazopanib) showed efficacy but limited by toxicity

Miller et al, Cancer Research 2010

Incidence

10 – 40%

Breast cancer patients undergoing axillary lymphadenectomy

Zuther JE. Lymphedema Management: The Comprehensive Guide for Practitioners. 2nd ed. New York, NY: Thieme; 2009.

Impact

Estimated US$2Bn

cost of treating breast cancer lymphedema to US healthcare system

From Shih, et al. J Clin Oncol. 2009 Apr 20; 27(12):2007-14.

CERES ONCOLOGY

Phase Ia and Ib in a single study

Monotherapy and Bevacizumab (Avastin®) combination evaluation

Solid tumour (advanced or metastatic)

No further treatment options

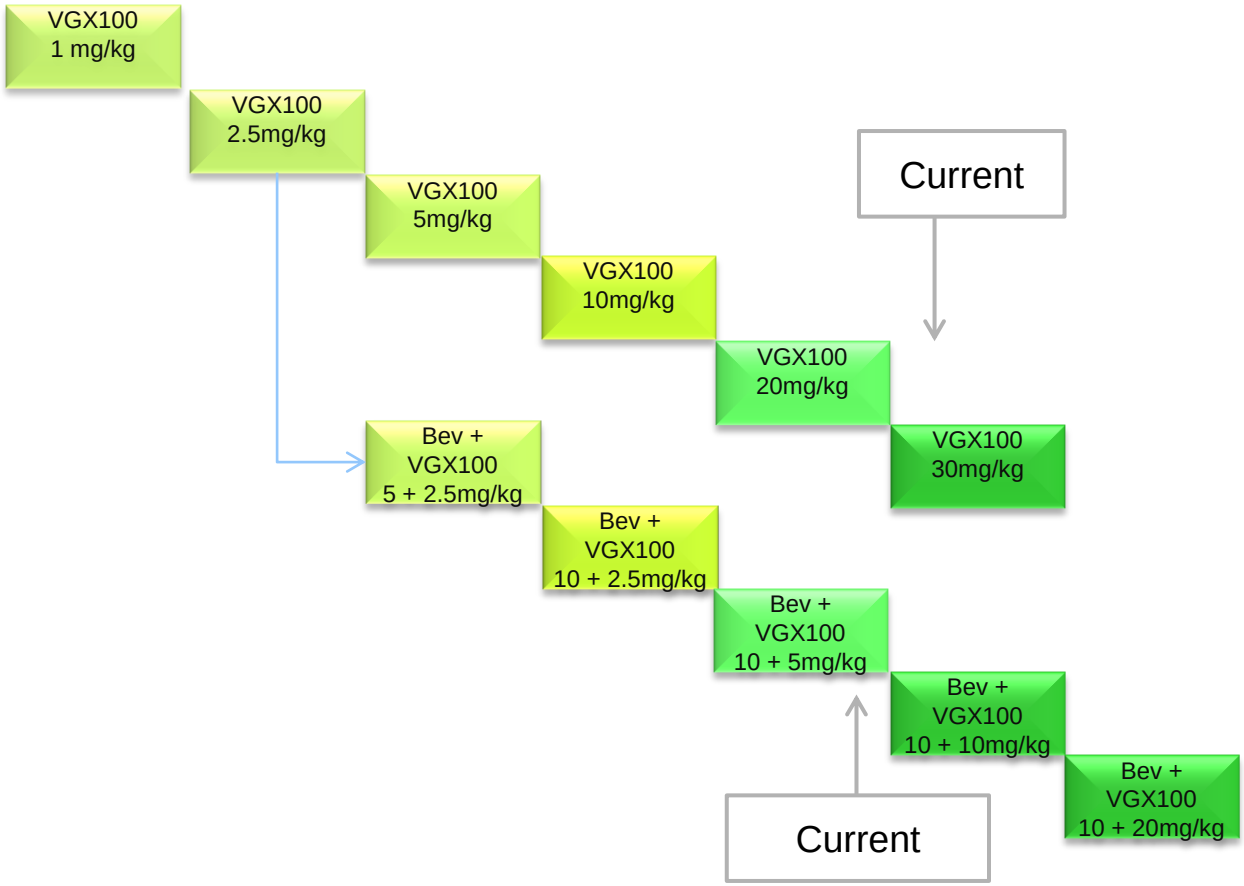
MD Anderson UCLA

"3+3" design

28 day DLT window

1º Safety
2º PK, HAHA, Biomarkers, Efficacy

Imaging every 8 weeks



- IND Q4, 2011
- Study start Jan, 2012

CERES ONCOLOGY

Phase 2 Lymphedema Clinical Study Design - VGX-100

- Proof of concept pilot study in patients with secondary lymphedema following breast cancer treatment
  - Open Label, single arm
  - VGX-100 monotherapy
  - Up to ~20 pts
  - Primary Endpoint: Improvement in Arm Volume
    - Response defined as >25% decrease in excess arm volume
    - Lymphedema measurements:
      - Arm volume
      - Interstitial Fluid Pressure (IFP)
      - Extracellular Fluid Volume (EFV)
  - Other endpoints
    - Safety and tolerability of VGX-100 in this patient population
    - QOL questionnaire (FACT-B+4 lymphedema questions)
- Hypothesis:
  - VGX-100 will demonstrate clinically meaningful benefit in patients with secondary lymphedema following breast cancer treatment

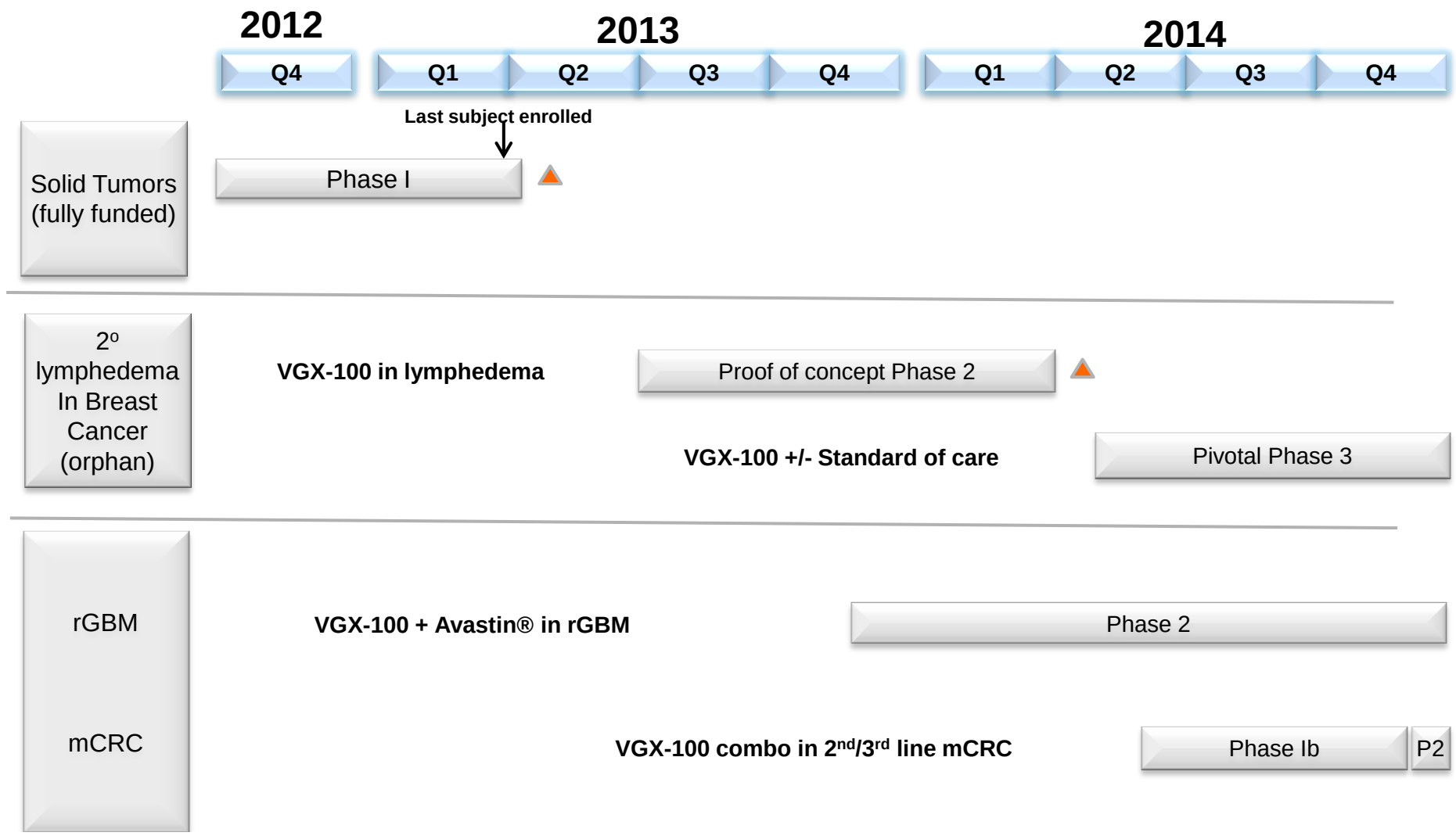
CERES ONCOLOGY

Phase 2 rGBM Clinical Study Design - VGX-100 + Avastin®

- Randomized comparator efficacy / safety study of VGX-100 + Avastin® versus single agent Avastin® in adult patients with recurrent glioblastoma multiforme following prior therapy.
  - Randomized
    - VGX-100 + Avastin® versus
    - Avastin® alone
  - Up to ~40 pts in each Tx group
  - Primary Endpoint:
    - Progression Free Survival at 6 months (PFS6) and Objective Response (complete or partial response [CR or PR]) as assessed by Macdonald criteria.
  - Secondary Endpoints:
    - Objective Response Rate and PFS6 as assessed by RANO criteria
    - Progression free survival (PFS)
    - Duration of response
    - Time to response
    - Overall survival (OS)
    - Safety
  - Other endpoints
    - Pre- and post-treatment changes in tumor blood perfusion measured by MRI

CERES ONCOLOGY

Forecast Timeline of Potential Value Creating Events



VGX-100: Strategic Imperatives, Critical Success Factors

Anchor in 2º Lymphedema of Breast Cancer	▪ Be the first therapy in secondary lymphedema of breast cancer
Expand in CRC, GBM & Beyond	▪ Prepare for proof of concept phase 2 studies ▪ Look for opportunities with combinations in other indications
Advance the Science of the VEGF-C pathway	▪ Biomarker strategy ▪ Optimising diverse therapeutic combinations with VGX-100
Ensure Drug Supply	▪ Manufacture for current/planned clinical studies ▪ Prepare for Phase 3 and commercial scaling

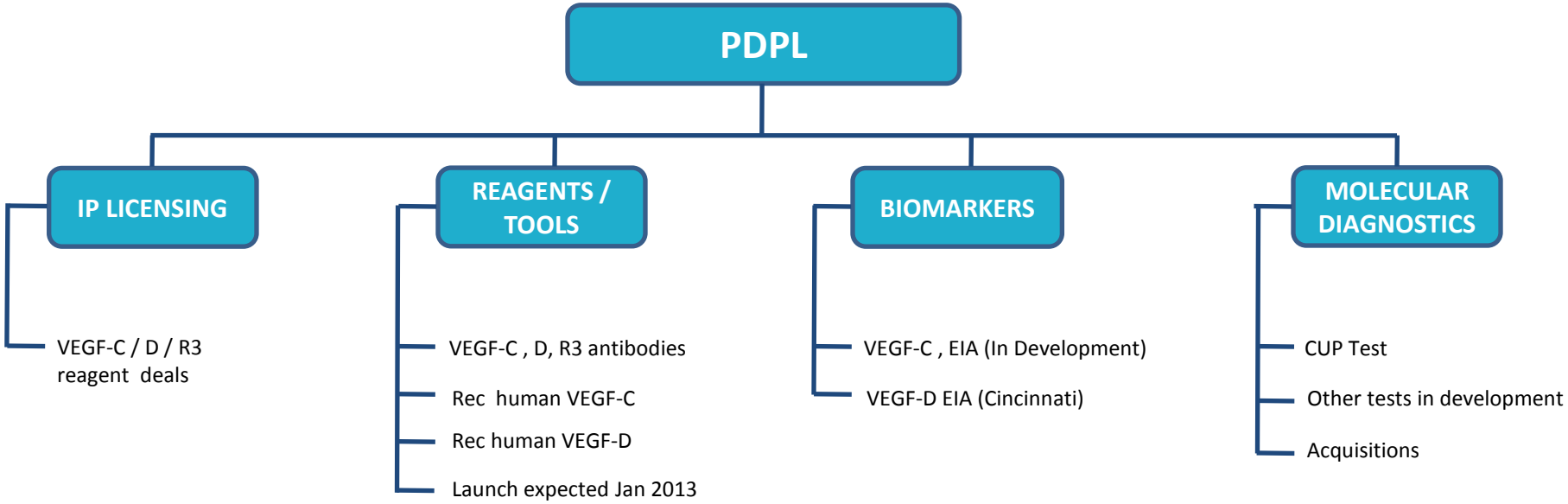
CERES ONCOLOGY

PRECISION DIAGNOSTICS PTY LTD

A research reagents and molecular diagnostics company

Precision Diagnostics
A Circadian Company

Precision Diagnostics Business Model



CUPGUIDE™

An aid in the diagnosis of Cancers of Unknown Primary Origin (“CUP”)

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
- Launched in Healthscope Territories October 2012
- Market size in Healthscope territories up to 10,000 tests p.a
- Pricing at $>1500 Potential Royalty $>1M p.a from 4 countries
- Partnership discussions in US/Europe ongoing
- Market in USA/Europe/Japan estimated to be 150,000 tests p.a
- 510K and CE Mark H1 2014

Development of a Gene Expression Based Assay to Determine the Origin of Metastatic Carcinomas of Unknown Primary.

Keith Byron[1], Lisa Paiman[1], Richard Tothill[2], Evangeline Buela[1], Fan Shi[3], Adam Kowalczyk[3], Robert Klupacs[4], David Bowtell[2]

[1.]Healthscope Advanced Pathology, Clayton, Vic, Australia, [2.]Peter MacCallum Cancer Centre, Melbourne, Vic, Australia, [3.]National (ICT) Australia, The University of Melbourne, Parkville, Vic, Australia, [4] Circadian Technologies Limited, Toorak, Vic, Australia.

Introduction

Carcinomas of unknown primary (CUP) account for 3–5% of all malignancies and are thus among the ten most-frequent cancers worldwide. The prognosis for patients with CUP is poor, with median survival of eleven months from the time of diagnosis. In light of the poor prognosis, morbidity and patient anxiety associated with extensive clinical investigations, the oncologist must decide how far to pursue identification of the primary tumour. However, when a primary tumour has been identified and specific treatment initiated, improved response rates and overall survival has been demonstrated.

Gene expression profiling using microarray technology has been demonstrated to be effective for the classification of cancer. A tumour's gene expression profile is believed to reflect the normal differentiated state of the cell of origin combined with the aberrant gene expression changes associated with disease transformation. It has also been shown that a tumour's gene expression signature is maintained even if the tumour has metastasised to a distant site and closely resembles that of the primary tumour.

Here we present stage one, of the development of a gene expression assay and tumour class prediction model to identify the site of origin of metastatic carcinomas of unknown primary.

Methods

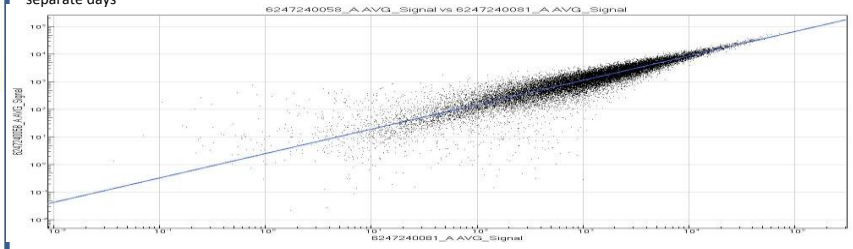
RNA extraction and processing: Seven micron sections of formalin fixed paraffin embedded (FFPE) tissue were first reviewed by a pathologist. Areas on the tissue containing the greatest amounts of tumour were macro-dissected to enrich to at least 80-90% tumour content. RNA from this tissue was then extracted using a modification of the Qiagen RNA Easy FFPE RNA extraction kit. Quantitation of RNA was then determined using the Quant-iT Ribo Green kit (Invitrogen) on a Nanodrop 3300 fluorimeter. RNA quality was assessed by amplifying a fragment (90 bp) of the highly expressed RPL13A ribosomal protein gene by reverse transcription PCR using an ABI7900.

Gene expression determination: Whole genome expression analysis was performed using the Illumina DASL humanHT-12-V4 BeadChip that is able to detect 29,285 coding and non-coding transcripts .
Data analysis: A binary Support Vector Machine was used as the basic classification method together with Recursive Feature Elimination as the feature selection method. To build a prediction model, cross validation on the training expression data was conducted, and the optimal number of genes selected, based on the greatest accuracy achieved.

Results

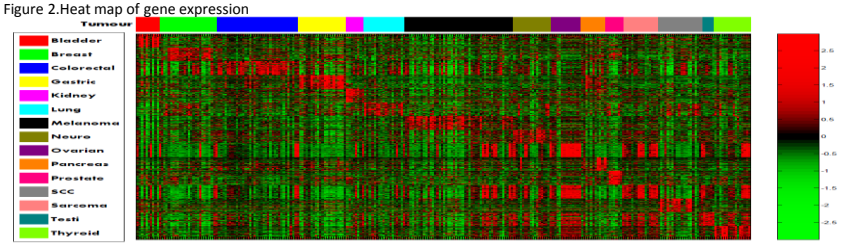
RNA was extracted from formalin fixed paraffin embedded samples containing known metastatic and primary tumours of various classes and varying degrees of differentiation. This set of samples comprised three hundred and ninety nine tumours of fifteen classes. All were analysed as described. To ensure reproducibility of gene expression detection, a control tumour sample was extracted then assayed on several occasions and on different days throughout the project. Figure 2 demonstrates representative raw intensity scatter plots of the control sample RNA run on separate days demonstrating good correlation.

Figure 1. Comparison of gene expression for the same sample extracted and analysed on separate days



To develop a classifier to predict tumour classes, we employed a one-versus-all classification strategy. For each of the 15 tumour classes considered, we built a classifier to distinguish each tumour class from all others. The discriminating probes for each of these 15 classifiers were selected by fitting the training data with a Support Vector Machine (SVM) method. In the testing phase, gene expression data from every tumour sample was tested in all of the 15 classifiers, and accordingly, one score that indicates the similarity of the test sample to a specific tumour class is produced. By comparing the similarity of the test sample to all tumour types, we are able to rank the probability of the test sample belonging to each tumour class.

Figure 2.Heat map of gene expression



In order to evaluate the accuracy of predictions made by the classifier, we employed a cross validation strategy. To do this, the training data was split randomly into five equal sized subsets, four of which were used to develop the classifier and one is used for testing. The training and testing process strictly follow the method described above, so that we obtain the ranked predictions for each test sample. The process is repeated five times, so that each subset is used for testing once. The accuracy of the predictions was then determined by comparing them with the known tumour types. The results of this strategy are demonstrated in table 1, where both overall accuracies and class-specific accuracies can be seen for the classifiers first prediction. Also demonstrated are the accuracies of the classifier correctly predicting the samples true tumour class in the first two and three predictions.

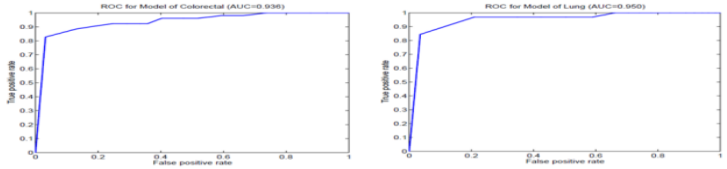
Table 1 : Classifier accuracies and specificities.

Tumour Class	N	Correct call with first prediction	Correct call within first two predictions	Correct call within first three predictions	Specificity
Overall Average		**83%**	**89%**	**93%**	**98.5%**
Bladder	13	85%	92%	92%	99.7%
Breast	56	79%	93%	96%	96.7%
Colorectal	48	85%	92%	96%	96.4%
Gastric	26	81%	85%	89%	99.2%
Kidney	14	93%	100%	100%	99.7%
Lung	30	83%	97%	97%	97.6%
Melanoma	50	78%	84%	88%	98.8%
Neuroendocrine	18	83%	89%	89%	98.7%
Ovarian	22	77%	96%	100%	98.4%
Pancreas	18	72%	78%	83%	97.7%
Prostate	19	89%	95%	95%	99.7%
Sarcoma	29	76%	83%	86%	96.6%
SCC	27	93%	93%	93%	99.2%
Testi	8	88%	88%	88%	99.7%
Thyroid	21	91%	91%	100%	100%

Area under ROC

The calculated area under the receiver operating characteristic (ROC) curve is a fundamental tool for diagnostic test evaluation. Here we have calculated the average area under the ROC curve across all 15 tumour classes to be 0.95 indicating a test of high diagnostic value. Class examples of ROC curve for both Colorectal and Lung can be seen in figure 3.

Figure 3. ROC curves for Colorectal and Lung tumour classes



Reproducibility of Predictions

To evaluate the reproducibility of the classifier, a single colorectal adenocarcinoma was analysed on four separate occasions. The gene expression data was then submitted to the classifier for prediction scoring. For all four samples submitted, the classifier correctly predicted the class to be "colorectal".

Conclusion

Although further validation is required using a independent test cohort of known metastatic tumours, as well as a cohort of samples from patients diagnosed with CUP, our data suggests that an expression-based diagnostic test could be effective in identifying the tumour of origin in patients presenting with CUP.

PERFORMANCE OF CUPGUIDE IS EXTREMELY GOOD

Table 1 : Classifier accuracies and specificities.

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Neuroendocrine	18	83%	89%	89%	98.7%
Ovarian	22	77%	96%	100%	98.4%
Pancreas	18	72%	78%	83%	97.7%
Prostate	19	89%	95%	95%	99.7%
Sarcoma	29	76%	83%	86%	96.6%
SCC	27	93%	93%	93%	99.2%
Testi	8	88%	88%	88%	99.7%
Thyroid	21	91%	91%	100%	100%

VEGF-D Diagnostics

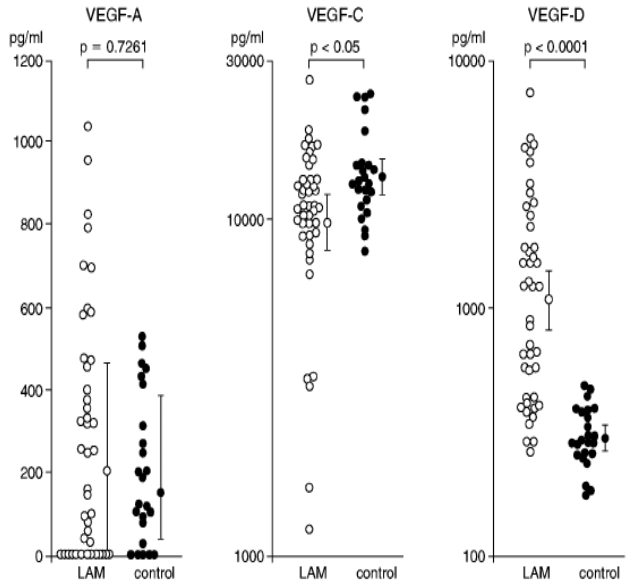
An aid in the differential diagnosis of Lymphangioleiomyomatosis (“LAM”) from other cystic lung diseases

VEGF-D Diagnostics in Respiratory Disease

- Lymphangioleiomyomatosis (LAM): A disease causing cystic lung lesions in women and has also been linked to genetic disease TSC
- VEGF-D has been shown to be a specific serum biomarker for LAM
- Often degenerative requiring lung transplant
- Frequently fatal
- Primarily affects women of reproductive age
- Estimated 50,000 cases worldwide plus approx 1M sufferers of TSC, but is assumed to be under-reported
- Test launched by Cincinatti Childrens's under CAP/CLIA Jan 2011
- Aiming for FDA approval and CE Mark H2 2013
- Possible extension to companion diagnostic use with mTOR therapy

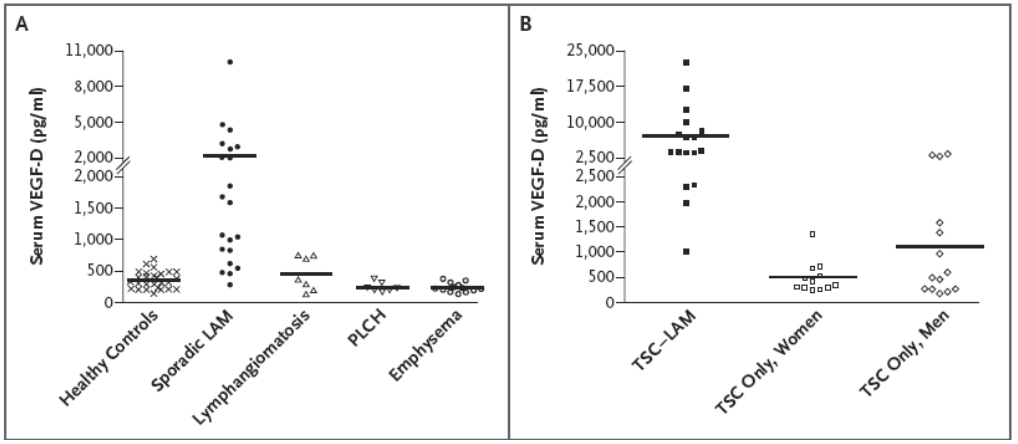
VEGF-D Diagnostics – Respiratory Disease

VEGF-D is increased in serum of patients with LAM



Seyama et al. Lymphatic Res & Biol., Vol 4, #3, 143-152, 2006

Serum VEGF-D levels distinguishable from other cystic and chylous lung diseases



Young et al. NEJM., 358(2), 199-200, 2008

VEGF-D – A biomarker for mTOR therapy?

OPEN ACCESS Freely available online

PLoS one

Multicenter Phase 2 Trial of Sirolimus for Tuberous Sclerosis: Kidney Angiomyolipomas and Other Tumors Regress and VEGF- D Levels Decrease

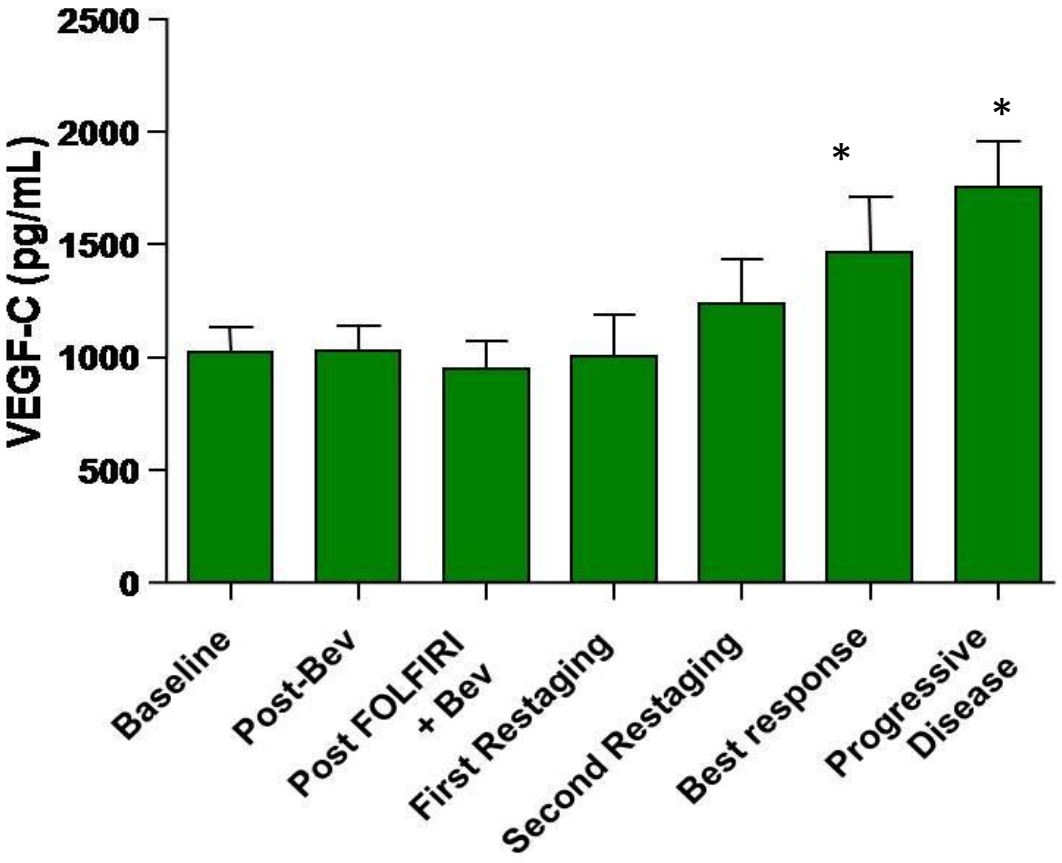
Sandra L. Dabora[1]*, David Neal Franz[4], Stephen Ashwal[5], Arthur Sagalowsky[6], Francis J. DiMario Jr.[7], Daniel Miles[8], Drew Cutler[5], Darcy Krueger[4], Raul N. Uppot[2], Rahmin Rabenou[8], Susana Camposano[2], Jan Paolini[2], Fiona Fennessy[3], Nancy Lee[9], Chelsey Woodrum[9], Judith Manola[3], Judy Garber[3], Elizabeth A. Thiele[2]

1 Biogen Idec Hemophilia, Weston, Massachusetts, United States of America, **2** Massachusetts General Hospital, Boston, Massachusetts, United States of America, **3** Dana-Farber Cancer Institute, Boston, Massachusetts, United States of America, **4** University of Cincinnati, Cincinnati, Ohio, United States of America, **5** Loma Linda University, Loma Linda, California, United States of America, **6** University of Texas Southwestern, Dallas, Texas, United States of America, **7** University of Connecticut, Hartford, Connecticut, United States of America, **8** New York University, New York City, New York, United States of America, **9** Brigham and Women's Hospital, Boston, Massachusetts, United States of America

VEGF-C Diagnostics

An aid in monitoring ongoing effectiveness of bevacizumab therapy in the oncology setting

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

C.Lieu et al., *"The Association of Alternate VEGF Ligands with Resistance to Anti-VEGF Therapy in Metastatic Colorectal Cancer (mCRC)"*, J.Clin.Oncol. 29:2011 (suppl; Abstract #3533).

VEGF-C Diagnostics Development

- Aiming for CLIA waiver availability H1 2014
- Aiming for FDA approval and CE Mark H2 2014
- Possible extensions to identify cancer patients at higher risk of metastatic spread

EXPECTED NEAR TERM MILESTONES

NEAR TERM MILESTONES

H1
2013

- **VGX-100 Phase 1 trials completed**
- **Ceres Oncology partnership**
- **Reagents Launch**

NEAR TERM MILESTONES

H2 2013

- **Opthea Partnership**
- **VGX-100 Phase 2 studies commenced**
- **IMC-3C5 Phase 1 studies complete**
- **VEGF-D FDA/CE Mark registrations lodged**
- **CUPGUIDE Northern Hemisphere registrations lodged**

NEAR TERM MILESTONES

H1

2014

- **VGX-100 Phase 2 oncology studies initial results**
- **VGX-300 IND Filed for “back of eye”**
- **CUPGUIDE FDA approval, CE Mark**
- **VEGF-D Diagnostic FDA approval**
- **VEGF-C Diagnostic CLIA waiver availability**

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Development Opportunity for VEGF-C Inhibitors in Wet AMD

Megan Baldwin, PhD

Chief Executive Officer

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Biotech Showcase (JPM), January 9 2013

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Opthea Pty Ltd

- Opthea Pty Ltd is a 100% owned subsidiary of Circadian Technologies, developing VEGF-C/-D/VEGFR-3 assets for eye disease.
- 'Seed' investment from Circadian Technologies.
- Actively seeking 'Series A' investment to achieve clinical proof of concept (Phase II completion) within 3 – 3.5 years.
- Developing biologic VEGF-C inhibitors for 'wet' AMD
  - Lead candidate: VGX-300 (soluble VEGFR-3)
  - 'Back-up' programs, 'back-up' candidates

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Wet (neovascular) AMD

Photos: The Angiogenesis Foundation

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IMPROVING ANTI-ANGIOGENESIS
A Major Commercial Opportunity

"Age-related macular degeneration (wet AMD) is a worldwide epidemic with an estimated prevalence of 30-50 million that rivals that of Alzheimer's disease and that of all cancers combined."

J.Ambati. The Cogan Lecture. IOVS, April 2011

Estimated $US 5 billion market opportunity p.a. in USA alone

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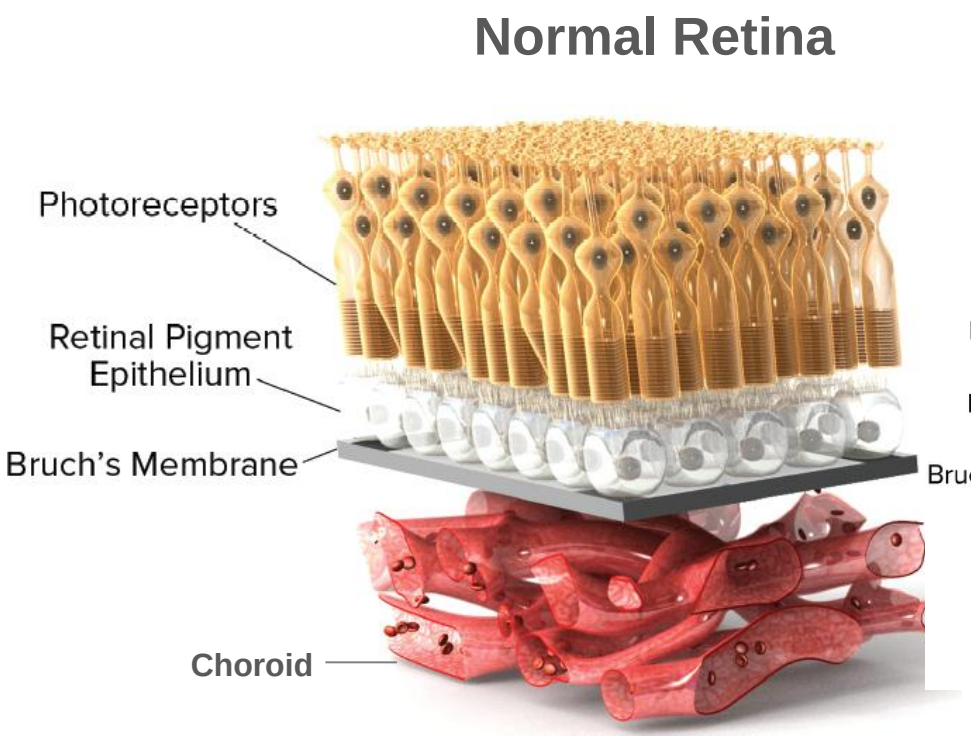
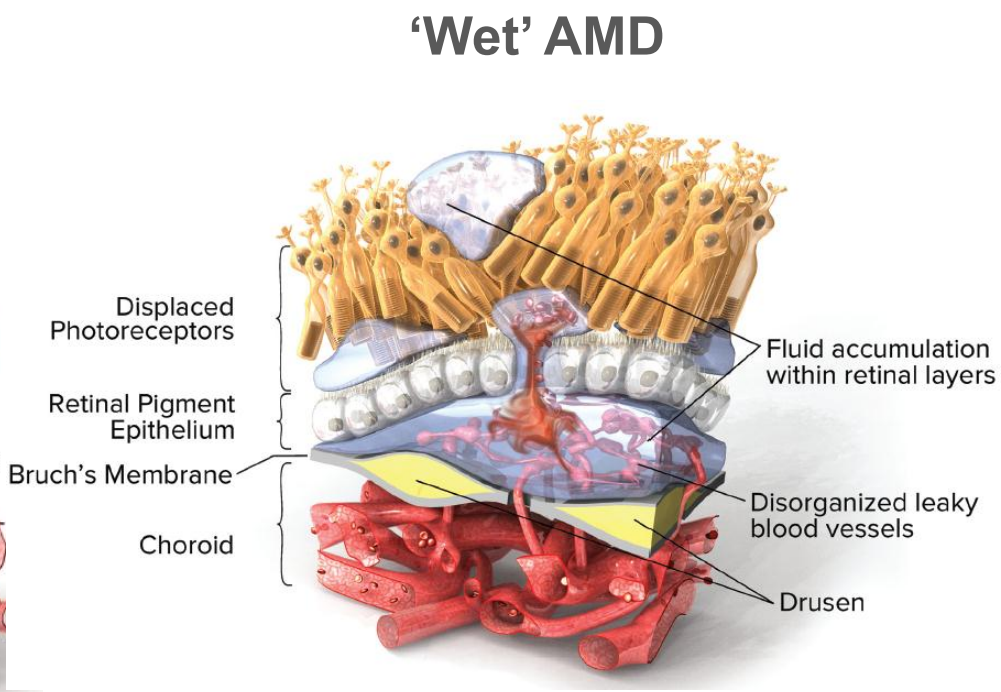
The Normal Retina and ‘Wet’ (neovascular) AMD





VGX-300 targets the two key processes in ‘wet’ AMD:

- Increased blood vessel growth
- Vessel Leakage

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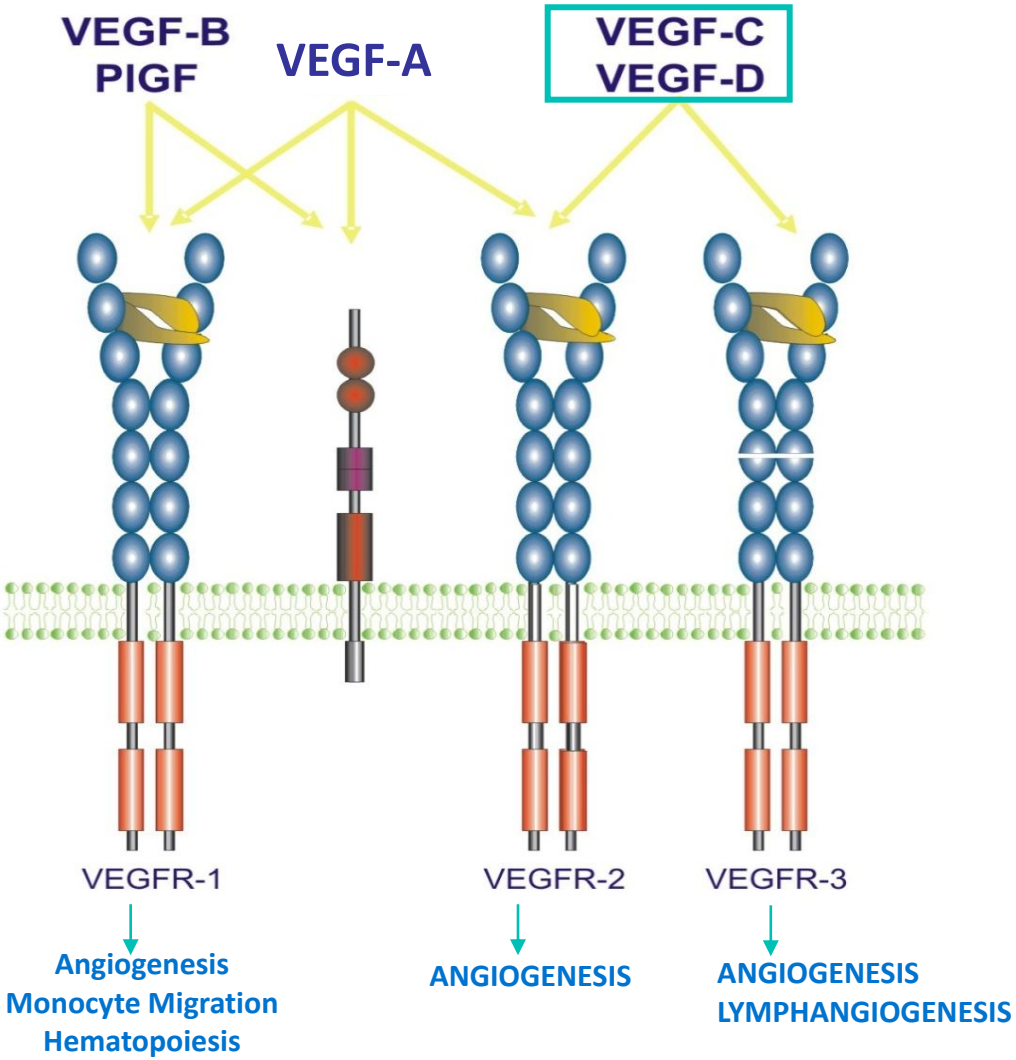
Figures: The Angiogenesis Foundation

VEGF-C & -D stimulate blood vessel growth and vessel leakage through VEGF-receptors



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IMPROVING ANTI-ANGIOGENESIS
A Major Commercial Opportunity

Existing therapies for wet AMD target VEGF-A but not VEGF-C:

- Only one-third of patients recover driving vision*
- One-sixth progress to registered blindness*

We are targeting 'sub' responders that experience no gain in vision & continue to leak:

- VEGF-C can induce angiogenesis and vessel leakage through the same receptor as VEGF-A.
- Combined VEGF-A/VEGF-C inhibition has the potential to improve patient response.

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* Ambati. IOVS. 52(5), 2011.

A Strong Intellectual Property Portfolio

- Circadian owns or controls intellectual property (IP) worldwide relating to therapeutic, diagnostic uses and biological antagonists of VEGF-C, VEGF-D and VEGFR-3.

- Opthea has an exclusive, worldwide, royalty-free license to develop inhibitors of VEGF-C/VEGF-D for eye diseases.
  - Secured ‘freedom to operate’
  - Long patent life extending to >2035 for lead VGX-300 molecule

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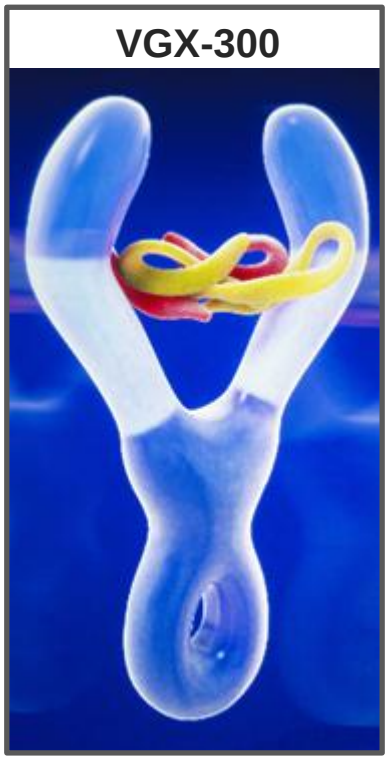
We are Targeting VEGF-C Blockade



VGX-300:

- Soluble receptor
- Neutralises both **VEGF-C & VEGF-D**
- Highly potent
- Soluble receptor in eye disease setting validated by approval of Eylea®.
- Eylea® and VGX-300 are similar in structure but bind <u>different</u> angiogenic factors.
- Combined administration of Eylea and VGX-300 shuts down **<u>all</u>** members of the VEGF family.

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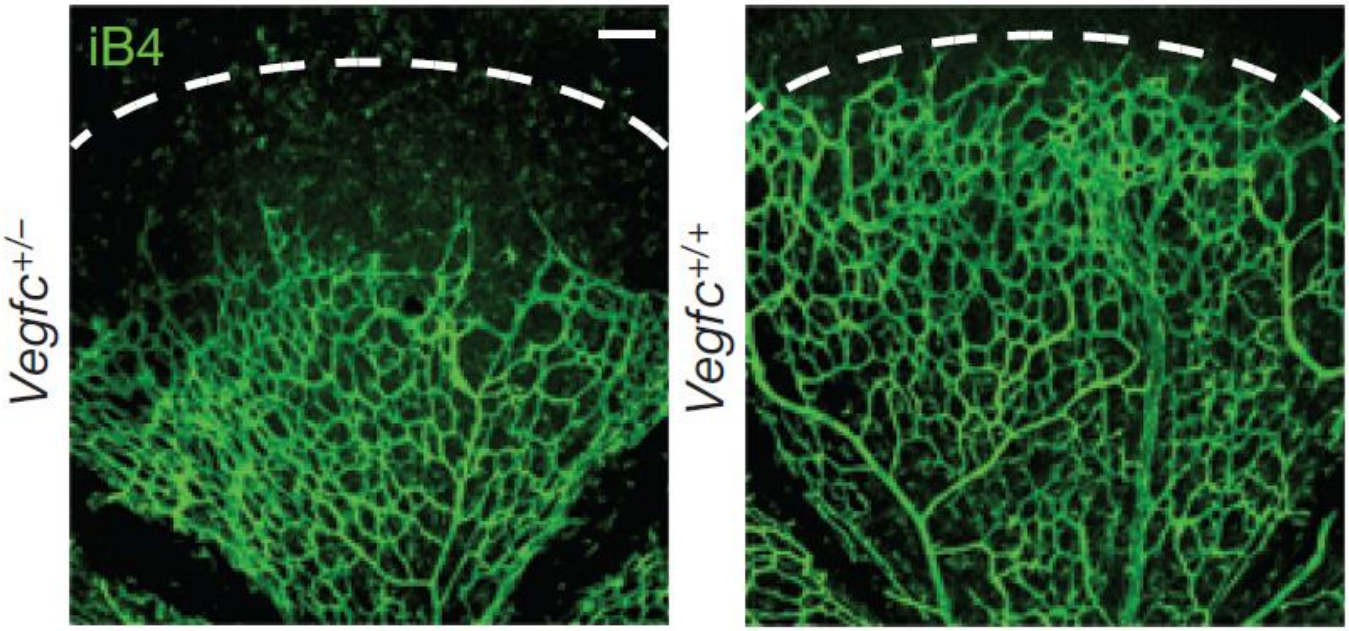
VEGF-C is Required for Retinal Vascular Development



Retinas from P5 VEGF-C+/- mice have reduced vascularity.

Tammela et al., Nature Cell Biology, 2011.

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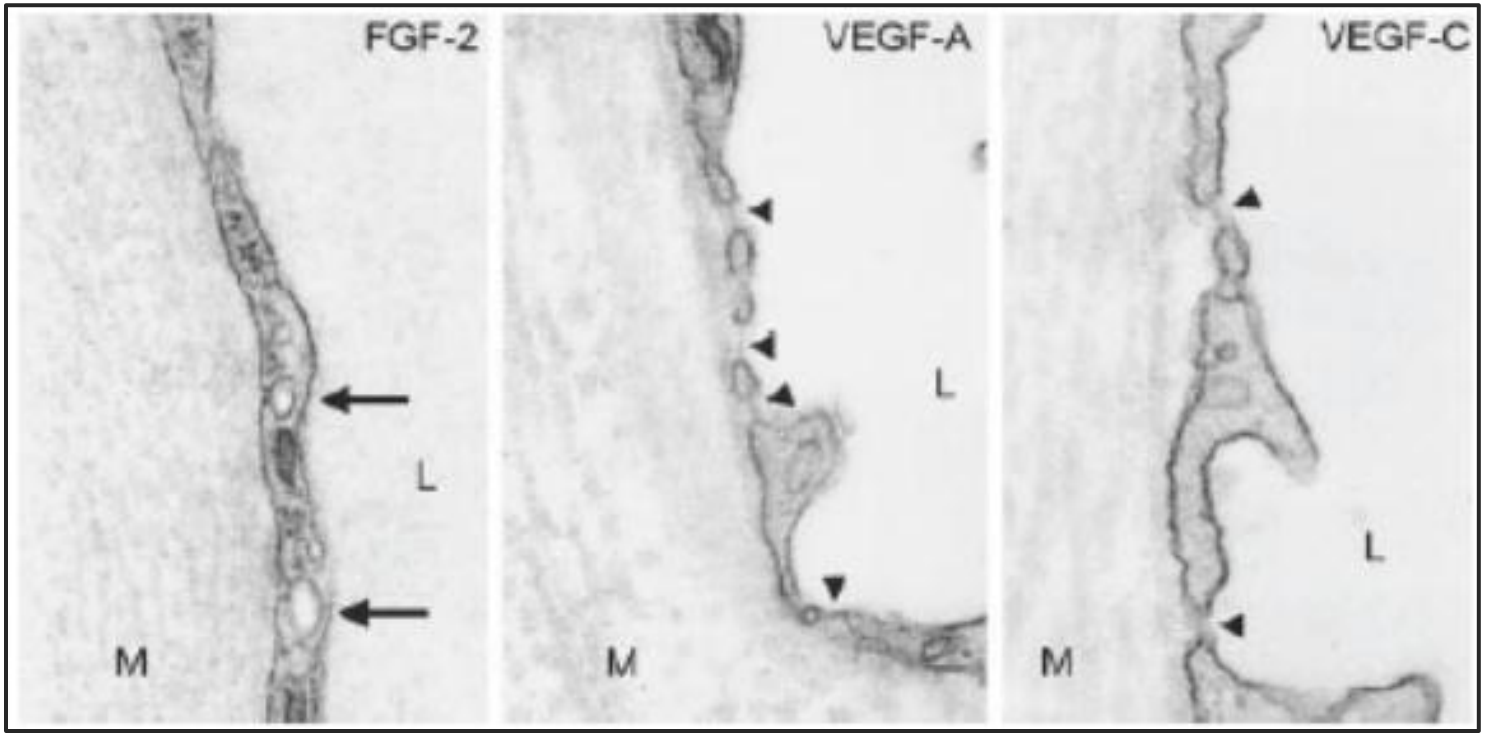
VEGF-C Induces Vascular Permeability - Contribution to Retinal Vessel Leakage



Cao et al,. Circ Res., 2004

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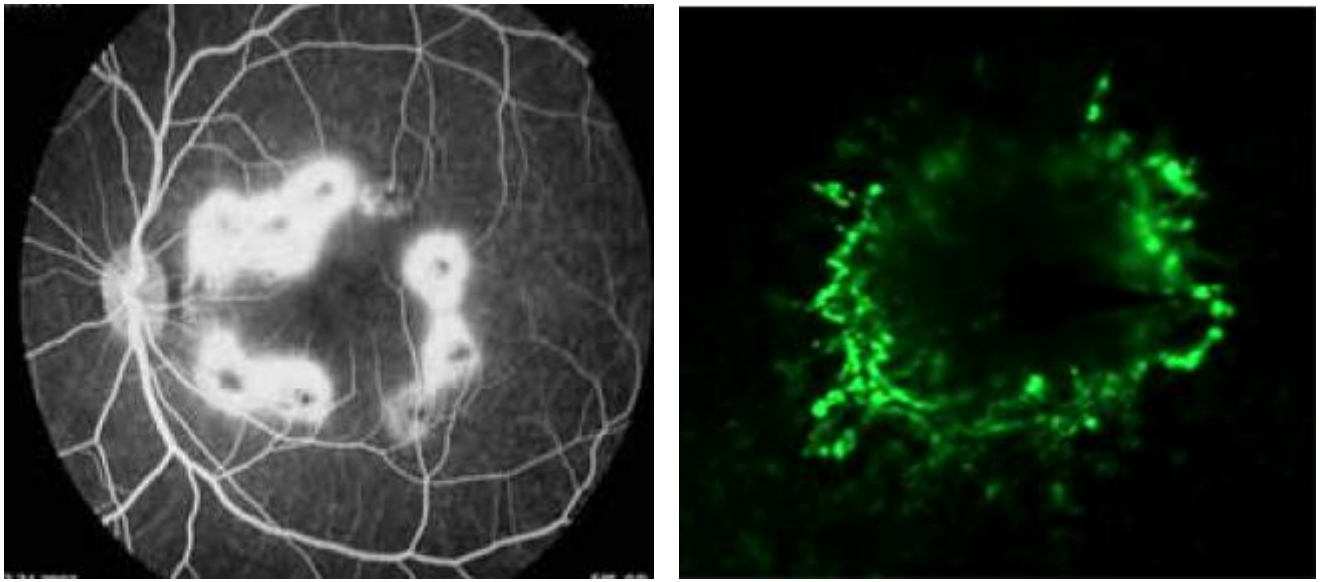
VGX-300 is Active in a Mouse Model of Wet AMD

- Laser induced CNV is the widely accepted model for preclinical drug testing for ‘wet’ AMD.



Laser induced CNV – fluorescein angiogram and immunohistochemical quantitation

- Features consistent with ‘wet’ AMD:
  - ✓ Penetration of Bruch’s membrane by choroidal vessels
  - ✓ Subretinal fluid accumulation
  - ✓ Leukocyte congregation
  - ✓ Fibrovascular scarring
  - ✓ Macrophage recruitment

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Development Activities

- We have demonstrated activity in rodent model of AMD
- We have shown comparable ocular biodistribution and PK profile in rabbits to marketed agents – potential for increased dosing interval in clinic
  - Fewer clinic visits & increased compliance
  - Key driver of market use
- Currently generating biomarker data for VEGF-C in ocular diseases
- Manufacture of clinical grade VGX-300 suitable for ocular administration commenced

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A Strong Team of Experienced Executives

- **Dr. Megan Baldwin:** PhD. Ex-Genentech. >15 years research & commercial experience in development of anti-angiogenesis/lymphangiogenesis agents.
- **Mr. Robert Klupacs:** BSc (Hons), Patent Attorney, Circadian CEO. IP expert
- **Dr. Mike Gerometta:** PhD. Ex-Agenix. >20 years biotechnology experience.
- **Ms. Susan Foran:** ex-GSK, ex-Kendle, Toxicology/Project Mgmt, >20 yrs experience.
- **Dr. Ian Leitch:** PhD. Ex.Miravant, Amgen. >15 years research & biotech management experience, specialising in PhI/II clinical trial strategy.
- **Dr. Robert Finger:** MD, PhD. Ophthalmologist specialising in retinal disease, clinical research & experience in clinical trials testing a-VEGF agents.
- **Ms. Susan Madden:** CFO.
- **Dr. Richard Chadwick:** Qualified European & Australian patent attorney.
- Opthea works with world-leading CROs experienced in Ophthalmological drug development and has relationships with world-leading Ophthalmological Research & Clinical Groups, including the Centre for Eye Research Australia (CERA) and Schepens (Harvard Medical School).

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Actively Seeking Investment and/or Partnership

- 'Seed' investment from Circadian Technologies.
- Seeking 'Series A' investment to reach clinical proof of principle.
- Unmet clinical need in 'wet' AMD based on sub-response to existing therapies targeting VEGF-A.
- Used in combination with a VEGF-A inhibitor, Opthea's VGX-300 results in more complete blockade of the most important pathway involved in 'wet' AMD progression.
- Great potential to improve patient responses:
  - vision gains, and
  - reduction in vascular leakage
- **Relatively short time (3.5 yrs) to clinical proof of concept.**
- Very large market opportunity.

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Thank-you