ANNUAL GENERAL MEETING 29 NOVEMBER 2013

Robert Klupacs, CEO and Managing Director

Circadian Technologies (ASX.CIR, OTCqx: CKDXY)

circadian

DISCLAIMER

Investment in Circadian Technologies Limited ('Circadian') is subject to investment risk, including possible loss of income and capital invested. Neither Circadian nor any other member company of the Circadian Group guarantees any particular rate of return or performance, nor do they guarantee the repayment of capital.

This presentation is not an offer or invitation for subscription or purchase of or a recommendation of securities. It does not take into account the investment objectives, financial situation and particular needs of the investor. Before making any investment in Circadian, the investor or prospective investor should consider whether such an investment is appropriate to their particular investment needs, objectives and financial circumstances and consult an investment advisor if necessary.

This presentation may also contain forward-looking statements regarding the potential of the Company's projects and interests and the development and therapeutic potential of the Company's research and development. Any statement describing a goal, expectation, intention or belief of the Company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercialising drugs that are safe and effective for use as human therapeutics and the financing of such activities. There is no guarantee that the Company's research and development projects and interests (where applicable) will receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this presentation. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning research and development programs referred to in this presentation.

CIRCADIAN TECHNOLOGIES LIMITED- 2012 AGM PRESENTATION OUTLINE

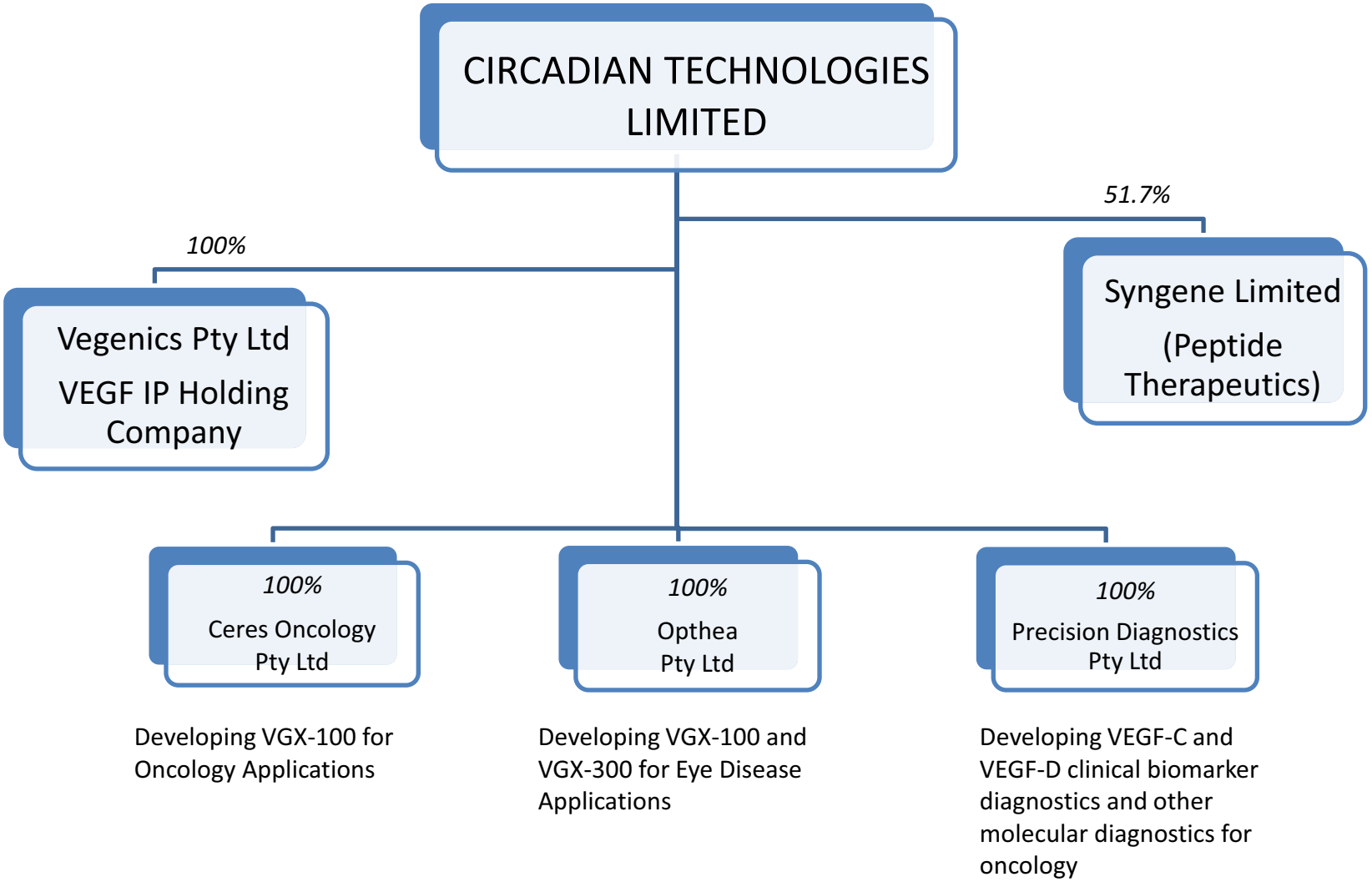
- **Corporate Snapshot & Structure**
- **Financials**
- **Status of Key Projects**
- **Expected milestones/value adding events next 6-18 months**
- **Ceres Oncology Pty Ltd**
- **Opthea Pty Ltd Presentation (Dr Megan Baldwin Opthea CEO)**

CORPORATE SNAP SHOT

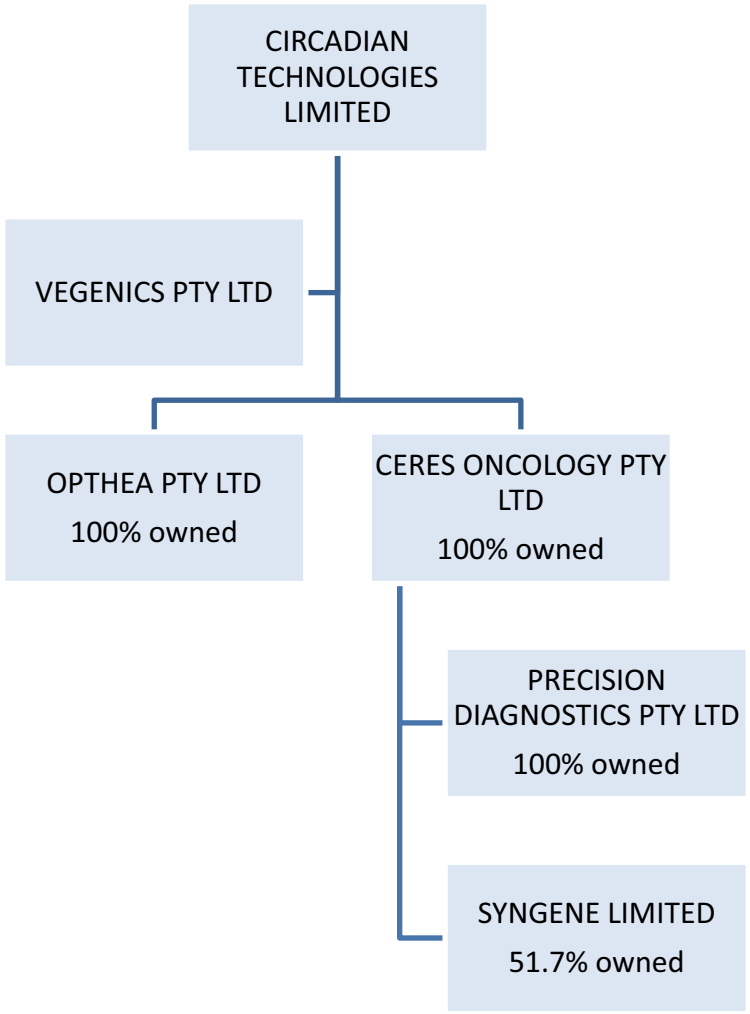
- Australian based emerging clinical stage company
- Developing human therapeutic and diagnostic products in cancer and eye disease through two 100% owned subsidiaries
- 3 therapeutic development products:
  - » VGX-100 & IMC-3C5 (oncology)
  - » OPT-302 (eye disease)

  - – Potential to improve upon clinical outcomes of Avastin®, Sutent ®, Nexavar®, Votirient®,Eylea® and/or Lucentis® >$12B of sales in 2012
  - – Unique opportunity to address diseases of cancer survivors – Lymphedema and to combine with existing therapies in solid tumours
  - – OPT-302 a major opportunity for single or combination therapy in AMD

CURRENT CORPORATE STRUCTURE



CORPORATE STRUCTURE CURRENTLY BEING FINALISED



CORPORATE SNAP SHOT

- Extensive and worldwide dominant intellectual property platform in respect of major biological targets
  - Over 400 granted patents worldwide in force up till 2023
  - Recognised by industry as “go to” company for VEGF-C inhibitors
  - “non-core” IP licensing to partners providing increasing revenues
- World class collaborators
  - Harvard
  - Johns Hopkins
  - UCLA
  - MD Anderson Cancer Centre
  - CSIRO
  - Ludwig Institute of Cancer Research
  - University of Helsinki
  - Peter Maccallum Cancer Institute
  - Centre for Eye Research Australia

OUR BUSINESS MODEL

A Business model of validating clinical concept and partnering further development after “de-risking” (very high value deal metrics)

- Key therapeutic development partnering events expected 2014
- Partnerships already in place:
  - Eli Lilly
  - Healthscope
  - Perkin Elmer
  - Bio-rad
  - Merck-Millipore

ANTIBODY THERAPEUTIC DEAL MAKING METRICS

Payments ($M) by stage at signing for mAb deals, January 2000–May 2011, outliers excluded*

Source: Deloitte Recap

Stage at Signing	Upfront + Equity	Upfront	Equity	R&D Payments	Total Milestones	# Deals
• **Phase III Average**	**$67.1**	**$29.7**	**$89.4**	**$137.5**	**$393.3**	**27**
• **Median**	**$31.0**	**$22.0**	**$25.0**	**$137.5**	**$250.0**	
# Deals Disclosing Data	12	12	5	2	9	
• **Phase II Average:**	**$41.5**	**$34.4**	**$11.6**	**$37.4**	**$262.3**	51
• **Median**	**$40.5**	**$27.7**	**$11.6**	**$28.3**	**$176.3**	
# Deals Disclosing Data	15	17	2	6	16	
• **Phase I Average**	**$38.9**	**$33.6**	**$3.5**	**$11.0**	**$333.6**	54
• **Median**	**$21.9**	**$21.9**	**$3.5**	**$11.0**	**$385.0**	
# Deals Disclosing Data	16	16	2	2	11	

NB Royalties not disclosed however industry averages
Phase 1 – 10-15%
Phase 2 – 12-25%
Phase 3 – 15-40%

FINANCIALS – CASH FLOWS

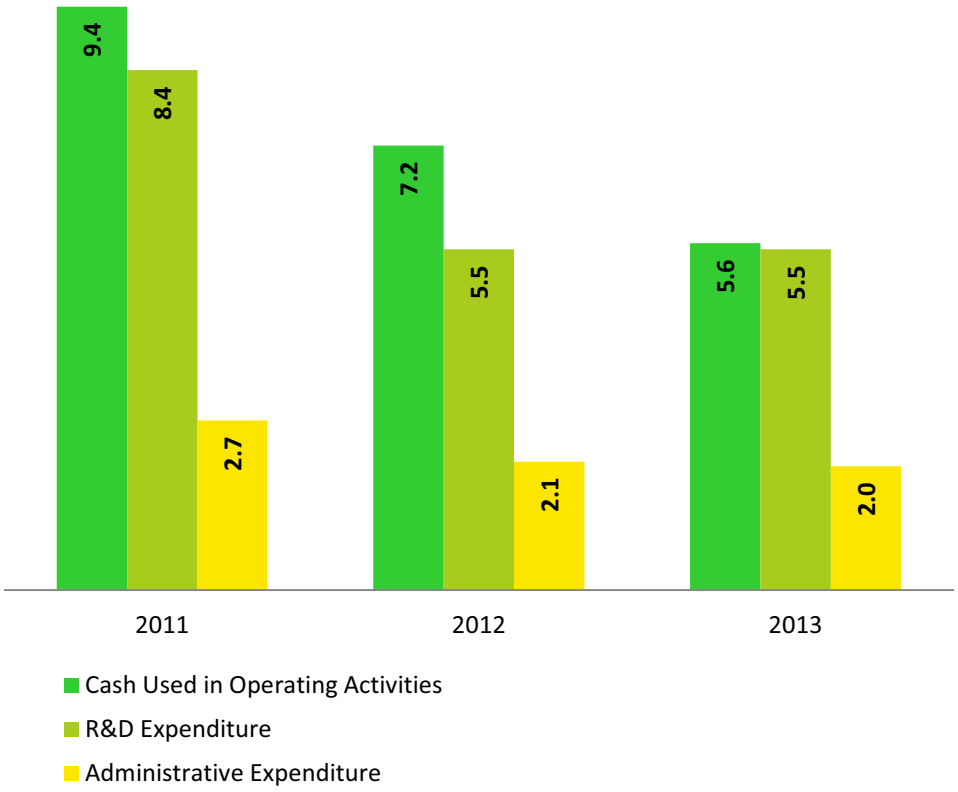
- Current Cash Oct 30 - $A9.0m (Unaudited)
- Value of Listed Holdings - $2.2M (Unaudited)
- Predicted Cash Burn (excluding items below)
  - 2014 FY - $6.0 - 8.0M p.a.
- Circadian Revenues (excluding interest)
  - est 2014 FY AUD $1.0M +
- Predicted cash burn does not take into consideration:
  - Increased R&D Tax Credit
  - Increased Royalties and partnering income
  - Income from divestment of investments

FINANCIALS

CASH AND EXPENDITURE

As of 30 June 2013

$ Million



Continuing reduction in admin

Expenses and focusing of capital to R&D

STATUS OF KEY THERAPEUTIC PROJECTS

VGX-100

- Phase 1a/b patient enrolment completed in 43 patients with advanced cancers
- Ongoing data analysis with presentation at major conference Q2 14
- Phase 2 studies planned to commence
  - lymphedema in Q1/2 2014 and recurrent glioblastoma multiforme in Q2/3 2014

IMC-3C5 (Eli Lilly)

- Phase 1 continuing

OPT-302

- Significant pre-clinical data in animal model of AMD
- Designated product development candidate
- Manufacturing commenced. IND Filing date target Q1 15

STATUS OF KEY DIAGNOSTIC PROJECTS

VEGF-D blood based diagnostic

- Currently marketed for LAM diagnosis and treatment monitoring in USA
- FDA designated kit as Humanitarian Use Device July 2013 in monitoring of LAM treatment
- Formal FDA and CE Mark registrations to be filed Dec 14
- FDA and CE Mark approvals expected Q2 14
- Ongoing clinical trials being undertaken in cancer and respiratory disease setting to obtain extended approved indications

CUPGUIDE™ (Healthscope)

- Launched in Australia.
- Sales lag while oncologist education undertaken.
- Very significant interest and number of leads. Sales ramp expected from Q1 14

KEY MILESTONES NEXT 6-18 MONTHS

Event	Expected Date
FDA Registration dossier and CE Mark application for VEGF-D Diagnostics lodged	Q4 2013
VGX-100 Phase 2a Trial Commencement in Breast Cancer Related Lymphedema	Q1/2 2014
VGX-100 Phase 1 Results formal presentation at major international oncology conference	Q2 2014
FDA and CE Mark Registration for VEGF-D Diagnostic	Q2 2014
VGX-100 Phase 2a Imaging Trial Commencement in recurrent glioblastoma multiforme	Q2/3 2014
VGX-100 Phase 2 Lymphedema Interim Trial Results	Q3/4 2014
OPT-302 Additional IND enabling studies commenced	Q2/3 2014
OPT-302 IND Filing	Q1 2015
OPT-302 Phase 1 Trial commencement in AMD patients	H1 2015
VGX-100 Phase 2a recurrent glioblastoma multiforme Imaging Trial Interim Results	H1 2015

CERES ONCOLOGY

A 100% owned subsidiary of Circadian Technologies Limited

"Developing VGX-100 as a single agent for treatment of breast cancer related lymphedema"

AND

"Developing VGX-100 in with combination anti-angiogenic and/or chemotherapy drugs to treat solid tumours"

Cancer Care: Large and growing need

- Cancer Incidence
  - 14.9 m in 2015 growing to 21.4 m by 2020 [1]
- Cancer Market
  - $64 Billion in 2012 growing to $120 Billion in 2020 [2]
- Key issues & Drivers
  - Cancer survivorship and ongoing treatment effects
  - Tailoring/Personalising therapy based on biomarkers/genomics
  - Chronic Care
  - Novel combinations
  - Aging

[1] American Cancer Society

[2] IMS Health

CERES ONCOLOGY

Ceres Oncology Development Opportunities

- Existing blockbuster anti-angiogenic therapies which block VEGF-A (Avastin, Sutent, Nexavar, Votrient)
  - Had combined sales >$10B in 2012
  - Limited by "resistance" and/or toxicities
  - Opportunities to improve patient clinical response, PFS and survival

- Strong scientific data that targeting VEGF-C in combination with existing therapies leads to enhanced anti-tumor responses

- Emerging evidence that VEGF-C is a key mediator involved in the pathophysiology of Breast Cancer Related Lymphedema.

CERES ONCOLOGY

Marketed Anti-Angiogenic Drugs: Blockbusters but with significant room for improvement

Drug	Approved Indication	Improvement in RR (%)	Improvement in PFS (months)	Improvement in OS (months)	2012 Sales ($US) TOTAL
Avastin (bevacizumab)	Metatstatic colorectal cancer (with chemotherapy) 	10 0 7.8 14.1	4.4 1.4 2.8 2.6	4.7* 1.4* 2.5* 2.0**	6.3b
	Metastatic non-squamous NSCLC (with chemotherapy)	20 10.3-14	1.7 0.4-0.6	2.0 NR*	
	Metastatic breast cancer (with chemotherapy) Only approved in Europe not USA	15.7 9-18 11.8-13.4 9.9	5.9 0.8-1.9 1.2-2.9 2.1	NS* NS* NS* NS*	
	Metastatic RCC	18 12.4	4.8 3.3	NS* NS*	
	Recurrent GBM	Only Phase 2 data published			
Sutent (sunitinib)	Metastatic RCC	35	6.0	4.6*	1.24b
Nexavar (sorafenib)	Metastatic RCC	8	2.7	NS*	1.02b
	Unresectable HCC	1 2	NS 1.4	2.8* 2.3	
Votrient (Pazopinib)	Metastatic RCC	27	5.0	NR*	0.44b

Modified from:
Carmeliet & Jain (2011)
Nature 473: 298-307

***-First Line**
****-Second line**

CERES ONCOLOGY

Ceres Major Assets

VGX-100 (Internal Development):

- Phase 1a & 1b patient enrolment completed Q4 2013.
- Phase 2a proof-of-concept trials to commence Q1/2 2014 in two indications:
  - Breast Cancer related Lymphedema
    - VGX-100 monotherapy
  - Recurrent glioblastoma multiforme (rGBM)
    - VGX-100 in combination with Avastin
- Phase 2a interim data available Q3/4 2014
- Additional clinical opportunities exist in mCRC & recurrent ovarian cancer
  - planned for late 2014 (earlier with partner)

IMC-3C5 (Imclone/Eli Lilly):

- Phase 1 complete H14.
- Phase 2 trials commence H1 15.

VEGF-D Diagnostic (Internal Development/On market in USA):

- FDA HDE registration filing Q4 13
- Approval expected Q2 2014

CUPGUIDE (Healthscope/On market in Australia):

- Molecular diagnostic for cancers of Unknown Primary

ROYALTY STREAMS:

- $550K p.a
- Imclone and research reagent companies – R&D Systems; Perkin Elmer; Bio-Rad; Santa Cruz; eBioscience; Millipore; Reliatech

CERES ONCOLOGY

VGX-100 – Multiple applications in oncology alone or in combination

Lead Product - VGX-100 a new monoclonal antibody to block VEGF-C

- Targets both blood and lymph vessel growth
  - Overcomes Avastin® (anti-VEGF-A) "resistance"
  - Enhances existing therapies:
    - Biologics, TKIs & Chemotherapy
    - Possibly immunotherapies
  - Specific opportunity in lymphatic diseases as well as solid tumours
  - Phase 2 ready from Q1 2014

Marketed anti-angiogenic therapies Avastin, Sutent, Nexavar, Votrient:

- Limited by "resistance" (Avastin) and/or toxicity profiles (TKI's)

Target Indications

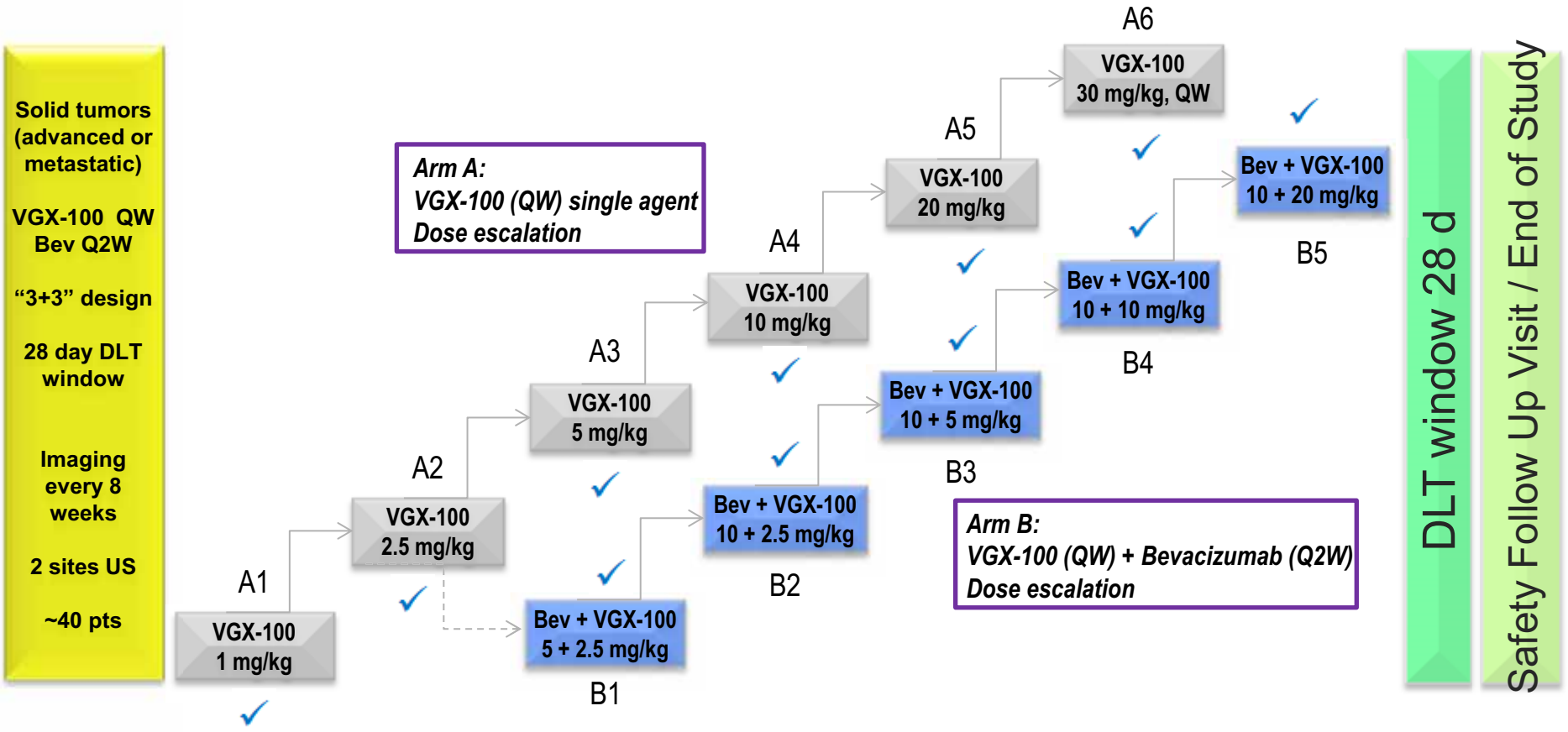
- ***VGX-100 monotherapy: Breast Cancer Related Lymphedema***
  - Major unmet need – possible large market
  - Rapid time to clinical proof-of-concept (Interim results Q4 14)

- ***VGX-100 combination with standard of care in oncology: Solid Tumours***
  - Recurrent Glioblastoma Multiforme ("brain cancer")
  - Recurrent Ovarian cancer
  - Metastatic Colorectal cancer
  - Gastric Cancer

CERES ONCOLOGY

VGX-100 Phase I study in 43 patients with advanced cancers

Two Arms: (1) Single agent and (2) In combination with Bevacizumab



Primary Endpoints

- Safety assessed by the incidence and severity of: AEs (including DLTs) & clinically significant changes in vitals, ECGs & safety Labs
- The recommended dose of VGX-100 alone and co-administered with bevacizumab

Secondary Endpoints

- Serum concentrations of VGX-100 and bevacizumab
- anti-VGX-100 antibodies
- Selected serum or tissue biomarkers: e.g. VEGF-A, VEGF-C, VEGF-D, soluble VEGFR-2, soluble VEGFR-3 etc
  Tumor response: measured by CT or MRI radiographic evaluation using RECIST 1.1 criteria

CERES ONCOLOGY

VGX-100 Phase 1 Interim results Summary

- VGX-100 is well tolerated in 43 adult patients with refractory advanced solid tumors:
  - Single agent (n=19 patients) at weekly doses up to 30 mg/kg
  - In combination up to 20 mg/kg, QW with Avastin® 5 or 10 mg/kg, Q2W (n=24 patients)

- Minimal overlapping toxicities when combined with bevacizumab (Avastin®)

- Preliminary Human PK data with VGX-100
  - Supports weekly dosing
  - Doses ≥ 20 mg/kg provide adequate coverage of VEGF-C inhibition
  - Combination with bevacizumab shows similar PK profile to that of either agent alone
  - No anti-VGX-100 binding or neutralizing antibodies
    - safety or pharmacokinetic profiles unaffected

- Early evidence of clinical activity
  - Interim tumour response data on the first 25 patients indicates:
    - ~one third of patients had a best response of stable disease
    - including some patients, who are refractory to standard treatments, showing a durable response ≥15 weeks.

- Further detailed evaluation of VGX-100 alone or in combination with Avastin® is ongoing

CERES ONCOLOGY

Clinical Program Overview of VGX-100 (anti-VEGF-C)

- **FIH Phase 1a/b clinical study: Enrolment Completed**
  - **Dose escalation study of VGX-100 +/- Bevacizumab in Advanced Solid Tumors**
    - 1º *Safety*
    - 2º *PK, Biomarkers, Tumor response by RECIST*
  - 43 patients enrolled
    - 19 pts single agent: at 1 - 30 mg/kg, QW
      - Well tolerated: no DLTs, no MTD
    - 24 pts in combination with bevacizumab: at 2.5 – 20 mg/kg, QW with Bev 5 or 10 mg/kg, Q2W
      - Well tolerated: one DLT (G3 HTN at lowest dose), no MTD

- **Phase II clinical planning:**

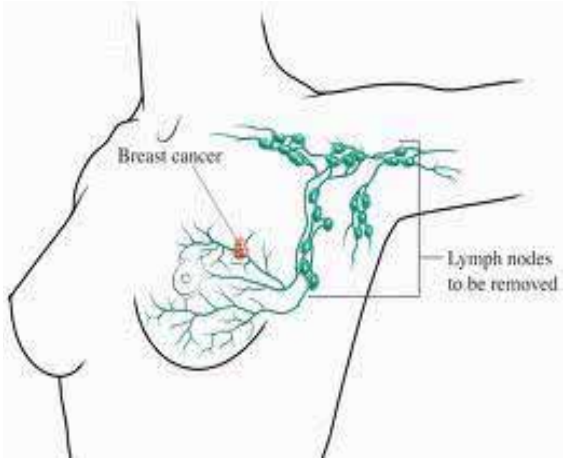
  - **Single agent in Breast Cancer Related Lymphedema (Study start Q1/2, 2014)**
    - Open label study in 15-20 patients
      - 1º *Improvement in Arm Volume - Response defined as >25% decrease in excess arm volume*
      - 2º *Interstitial Fluid Pressure, Extracellular Fluid Volume using BIS (L-Dex® U400; Impedimed), Safety, PK, Biomarkers, QOL questionaire (FACT-B + 4 lymphedema)*
    - Interim results Q3, 2014

  - **Combination with bevacizumab in Recurrent GBM (Study start 2014)**
    - 2 part study
    - Part 1 tumor perfusion imaging (DCE-MRI) study in 12 patients
      - 1º *Vascular "normalization index", reduction of vascular permeability - decrease in volume transfer constant (Ktrans), changes in micro-vessel volume, Edema alleviation*
      - 2º *Clinical benefit outcomes: ORR, APF6, PFS, OS*
    - Part 2 RCT study of VGX-100 + bevacizumab versus bevacizumab alone in 80 patients
      - 1º *ORR, PFS and OS*
      - 2º *OS*

CERES ONCOLOGY

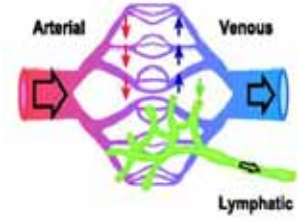
VEGF-C involved in Pathophysiology of Secondary Lymphedema in Breast Cancer

Lymph node surgery +/- radiation can lead to **lymphatic vessel dysfunction**

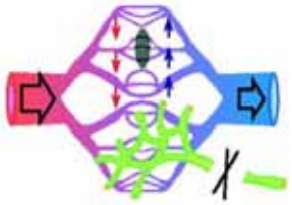


Lymphatic vasculature

Normal fluid homeostasis



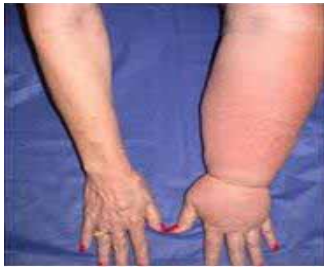
Lymphatic dysfunction



USA: 230,000 new cases of breast cancer annually & 2.6M survivors of breast cancer (2011, NCI)

Norrmén C et al. Circulation 2011;123:1335-1351

~25% of women will develop **secondary lymphedema**



- Blocked lymphatic function can lead to fluid edema in arm.
- Swelling can cause pain, reduced function & decreased QOL
- Latent period to onset - median within 1st year.
- Severity classified as stages 1-3
- Current treatments:
  - Massage &/or Compression therapy
  - *No drug therapy approved*

- **VEGF-C is elevated in patient population**
- **SNP genotyping: VEGF-C, VEGFR-2/3 involved in lymphedema development and severity**
- Lymph flow decrease detected by interstitial cells results in a compensatory increase in VEGF-C
- Leads to ↑vascular permeability & fluid filtration,a rise in interstitial pressure & some restoration of flow, but at the expense of ↑volume / edema

Same concept applies to ovarian, prostate, bladder cancers but leads to lower limb edema

CERES ONCOLOGY

VGX-100 a significant opportunity in Breast cancer treatment related Lymphedema

- **There are currently no approved drug therapeutics for this condition**
- **VEGF-C shown to be significantly increased in lymphedema patients compared to unaffected controls**

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

"…Samples were available for 16 pts with chronic lymphedema and 24 matched controls. Median VEGF-C levels were significantly increased in pts with lymphedema.."

- **Non-selective VEGF-C receptor blocker (pazopanib, GSK) showed efficacy but limited by toxicities associated with TKIs**

Miller et al, Cancer Research 2010 – 50% of patients respond

"..Ten pts were enrolled… three pts discontinued therapy prior to the first post-treatment assessment. Five pts met the definition of response with a 25% reduction in excess arm volume four weeks after initiating treatment. …."

CERES ONCOLOGY

Breast Cancer Lymphedema statistics and possible market

- USA – 230,000 new cases of breast cancer annually (2011, NCI)
- USA – 2.6M survivors of breast cancer (2011, NCI)
- Estimated that 10-50% of these will have lymphedema
- Estimated cost of treating breast cancer lymphedema to US healthcare system >$US2B p.a
- **NB – Lower limb Lymphedema associated with ovarian, uterus, prostate cancer treatment occurs in around 10-20% of patients.**

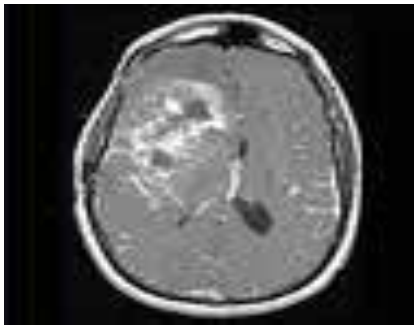
CERES ONCOLOGY

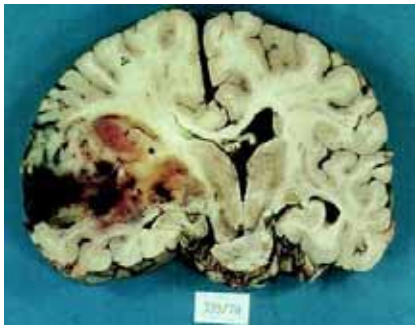
Phase 2a Lymphedema Clinical Study Design - VGX-100

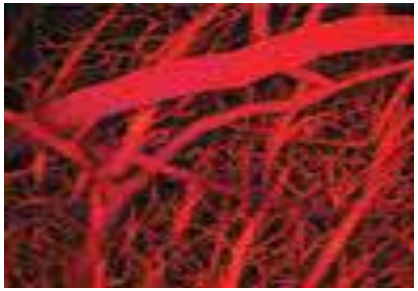
- **Proof of concept open label trial in patients with secondary lymphedema following breast cancer treatment**
  - **VGX-100 monotherapy**
    - 20 mg/kg, QW
  - **15-20 pts**
    - Females ≥ 18 yrs with unilateral lymphedema attributed to prior surgery or radiation therapy for breast cancer
  - **Primary 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) using bioelectrical impedance analysis
  - **Other endpoints**
    - Safety & Tolerability of VGX-100
    - Biomarkers (including VEGF-A, VEGF-C, VEGF-D, soluble VEGFR-2, and soluble VEGFR-3); Genotyping of SNPs for VEGF-C, VEGFR-2 and VEGFR-3
    - QOL questionaire (FACT-B + 4 lymphedema)
- **Sites**
  - 2-3 sites in the USA
- **Hypothesis:**
  - VGX-100 will demonstrate clinically meaningful benefit in patients with secondary lymphedema following breast cancer treatment

CERES ONCOLOGY

VGX-100 opportunity in recurrent Glioblastoma multiforme (rGBM)







- GBM is complex due to genetic mutations that occur
  - *e.g P53, EGFR, **VEGF**, MDM2, MGMT*
- Of all the mutations - **upregulation of VEGF appears to be of upmost importance**
- High grade gliomas are **highly vascularized tumors**
- GBM has **high expression of VEGF ligands and receptors** compared to lower level tumors and normal brain tissue
  - **associated with poorer prognosis**
- The resulting increase in vascular permeability & endothelial gaps **allows for rapid growth of the tumor**

- **Primary GBM median survival ~ 14.6 mths**
  - with best SOC
    - (surgery + radiotherapy & temozolomide)
- **Recurrent GBM survival ~3 - 6 mths**
  - Avastin has shown an ORR of ~26-28% & a response duration of 4.2 months in a pivotal Phase 2 trial of rGBM (Cohen et al, 2009).
- **GBM represent 2% of cancer deaths**
- **Ranks 1st among tumors for "life years lost"**
- **Major unmet medical need**

Wen et al, NEJM, 2007, 13, 1253
Peles et al, Neurosurgery, 2004, 55, 566
Stupp R et al, J Clin. Oncol. 2002; 20: 1375
Vredenburgh J & Wen PY, Clin. Care Options Oncol., 2008
Burnet N et al., Br. J. Cancer, 2005; 92: 241
Schwartzbaum J et al., Nature Clin. Practice Neuroncol., 2006; 2: 494

CERES ONCOLOGY

VGX-100 Phase 2 rGBM study: Key Design Elements

- Eligible patients: Recurrent Glioblastoma multiforme (rGBM)
  - 1st or 2nd recurrence

- Part 1: Open Label Tumor Imaging Study
  - Two sites in Australia
  - Up to ~12 patients
  - VGX-100 (QW) +/- Avastin (Q2W)
  - Dynamic contrast enhanced MRI tumor perfusion imaging – neuroimaging Biomarker of response
    - Vascular "normalization index"
    - reduction of vascular permeability - decrease in volume transfer constant (K^{trans})
    - changes in microvessel volume
    - Edema alleviation
    - Correlate to clinical benefit outcomes: ORR, APF6, PFS, OS

- Part 2: Expand to P2 randomized study in ~80 pts with rGBM:
  - Avastin alone vs VGX-100 + Avastin
  - ORR, PFS and OS

CERES ONCOLOGY

Thank you

www.circadian.com.au

Developing OPT-302 (formerly VGX-300): A VEGF-C/VEGF-D "Trap" for Wet AMD

Megan Baldwin, PhD
Chief Executive Officer
megan.baldwin@opthea.com

Disclaimer

This presentation has been prepared by Opthea Pty Ltd ("Opthea") on a confidential basis. This presentation is supplied subject to the conditions outlined below ("Conditions"). The receipt of this presentation by the recipient evidences its acceptance of the Conditions.

This presentation is based on information obtained from sources believed to be reliable but is not guaranteed as being accurate and does not purport to contain all the information that the recipient may require to evaluate Opthea and its business. The information in this presentation is subject to change without notice. Opthea (including its advisers, directors, employees, consultants, related bodies corporate and the directors, shareholders, managers, employees or agents of any of them) (the "Information Providers") shall not be under any obligation to correct, update or revise this presentation or any written or oral communications transmitted to the recipient.

This presentation is not a recommendation by the Information Providers that the recipient acquire securities in Opthea, or that securities in Opthea are a suitable acquisition for the recipient. The recipient should conduct its own independent investigation and assessment of the contents of this presentation and the merits of an investment in the securities of Opthea.

The Information Providers make no representation or warranty (whether express or implied) as to the accuracy, reliability, reasonableness or completeness of this presentation or its contents. All of the Information Providers expressly disclaim any and all liability (including for direct or consequential losses, and whether arising from negligence or otherwise) for, or based on, or relating to any such information (including estimates or forecasts) contained in this presentation, or for any errors in or omissions from this presentation, except for any liability which cannot be excluded as a matter of law.

This presentation may contain certain forward-looking statements, forecasts, estimates, projections and opinions ("Forward Statements") prepared by the Information Providers. No representation is made or will be made by any of the Information Providers that any Forward Statements will be achieved or will prove to be correct. Actual future results and operations could vary materially from the Forward Statements. Similarly, no representations are given by the Information Providers that the assumptions disclosed in this presentation upon which Forward Statements may be based are reasonable.

This presentation does not constitute investment, accounting, financial, legal or tax advice.

This presentation is made available to the recipient for information purposes only and is not a disclosure document for the purposes of the Corporations Act 2001 (Cth) and is not an offer or invitation to any recipient or any other person to acquire securities in Opthea. Offers to subscribe for securities may be made by Opthea in due course to recipients on the basis that recipients are 'sophisticated investors' or 'professional investors' within the meaning of the Corporations Act 2001 (Cth). Recipients may only accept the offer by signing and returning the acceptance form provided with the offer.

The information in this presentation is confidential and must not be copied, reproduced or distributed to others at any time. The Information Providers do not accept any liability for any loss or damage of any kind arising out of the use or unauthorised reproduction, distribution or transmission of any part of this presentation.

OPTHEA

OPTHEA

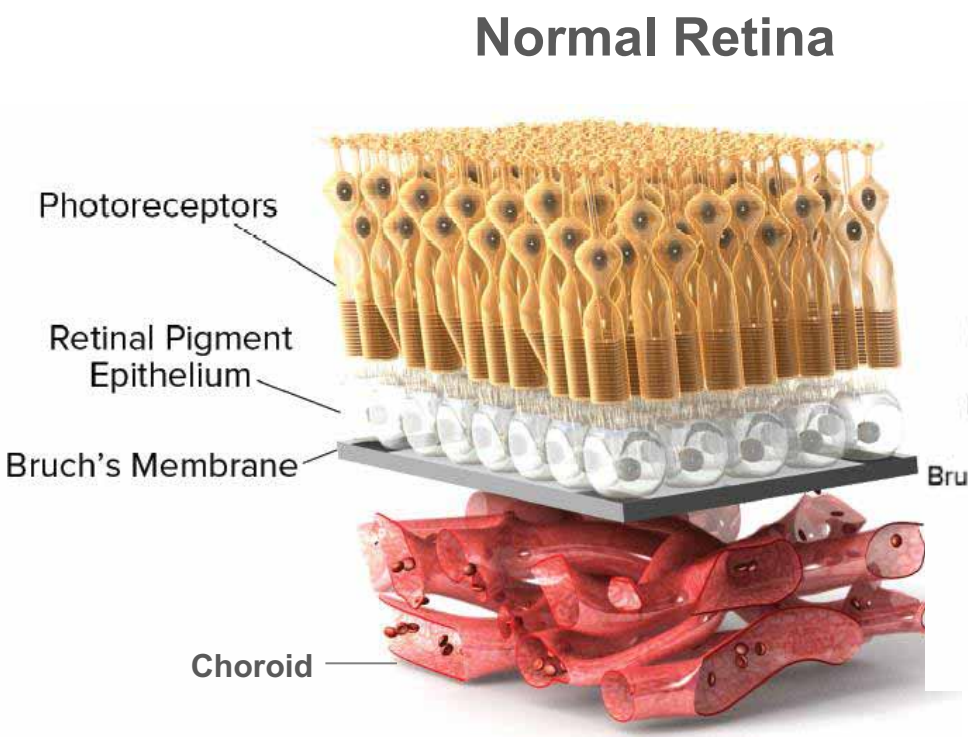
- Created Sept ‘12 to develop biologic inhibitors of VEGF-C for the treatment of eye diseases.
- Exclusive, world-wide rights from Circadian to a large IP patent estate covering biologic inhibitors of VEGF-C and VEGF-D for the treatment of eye disease.

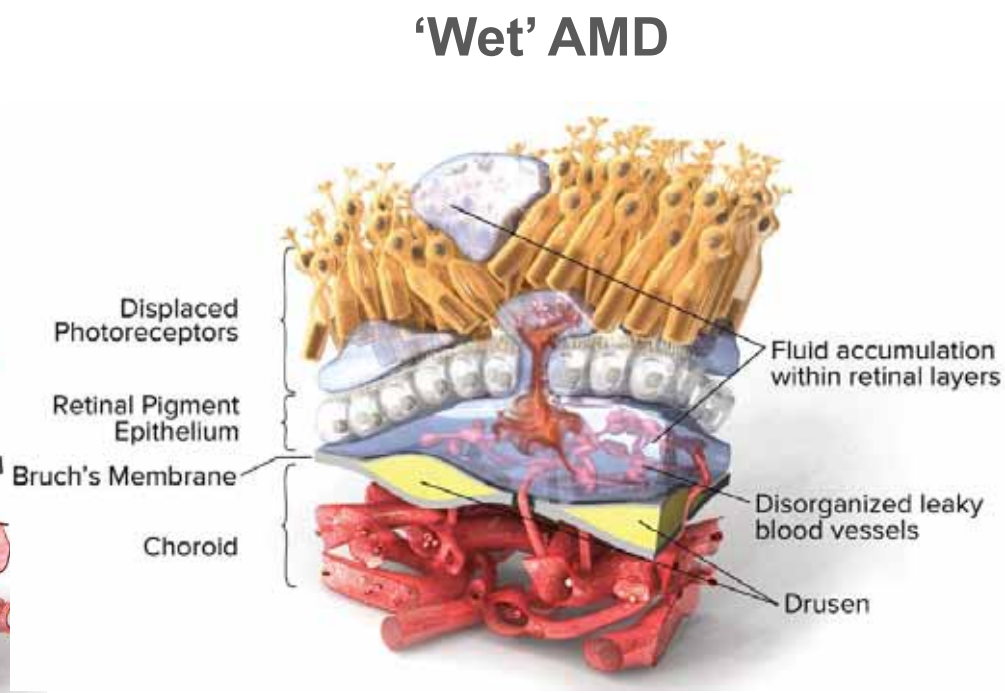
Opthea's ophthalmology program

- **Lead molecule:**
  - OPT-302 (soluble VEGFR-3, VEGF-C/-D 'Trap')
- **Mechanism:**
  - Blocks VEGF-C and VEGF-D:
    - Inhibits blood vessel growth
    - Inhibits vessel leak
- **Strategy:**
  - To develop OPT-302 for use in combination with existing VEGF-A inhibitors for the treatment of wet AMD
  - Achieve more complete blockade of the VEGF pathway

OPTHEA

The normal retina and ‘Wet’ (neovascular) AMD





Figures: The Angiogenesis Foundation

Wet (neovascular) AMD

Figures: The Angiogenesis Foundation

OPTHEA

Wet AMD is a major commercial opportunity

"Few people are aware that macular degeneration is an incurable eye disease and that it is the leading cause of blindness for those aged 55 and older in the United States" …
American Macular Degeneration Foundation

- Estimated $5B p.a. market opportunity in wet AMD in US alone
- Increasing with aging population

- Only two targeted therapies approved for wet AMD
- Both target VEGF-A
  - Roche/Novartis: **Lucentis®**
  - Regeneron/Bayer: **Eylea®**
  - Roche/Genentech: Avastin® (off-label use)
- Lucentis® and Eylea® tracking to >5BN in 2013 sales

OPTHEA

An unmet medical need remains despite anti-VEGF-A therapy

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*
- >50% of patients do not experience significant gain in vision

We are targeting 'sub' responders:

- Wet AMD patients that experience no gain in vision & continue to leak following Lucentis®/Eylea® therapy
- Combined VEGF-A/VEGF-C inhibition has the potential to improve patient response

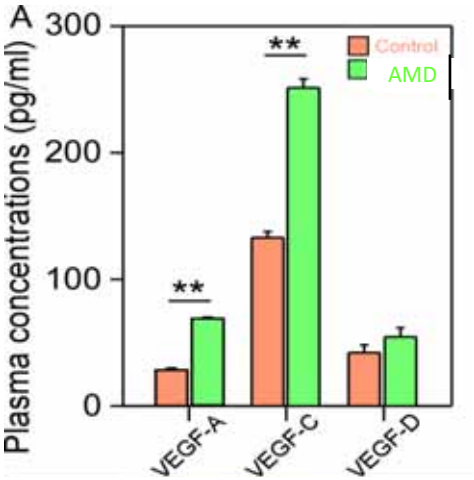
* Ambati. IOVS. 52(5), 2011.

OPTHEA

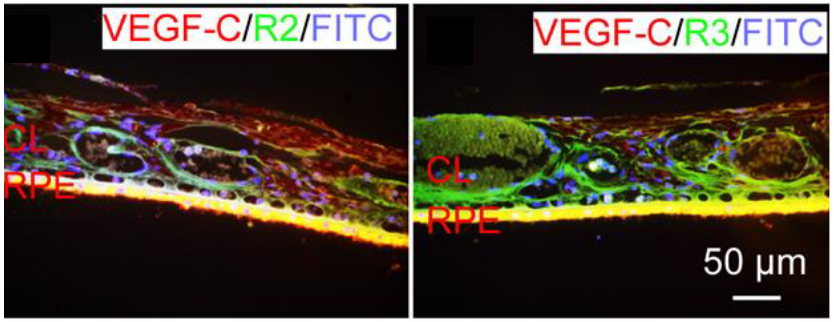
Elevated VEGF-C in wet AMD patients

- VEGF-C is involved in retinal vascular development and disease
  - Under-expression of VEGF-C disrupts retinal vasculature development
  - Elevation of VEGF-C associated with wet AMD

Circulating VEGF-C levels significantly elevated in AMD patients

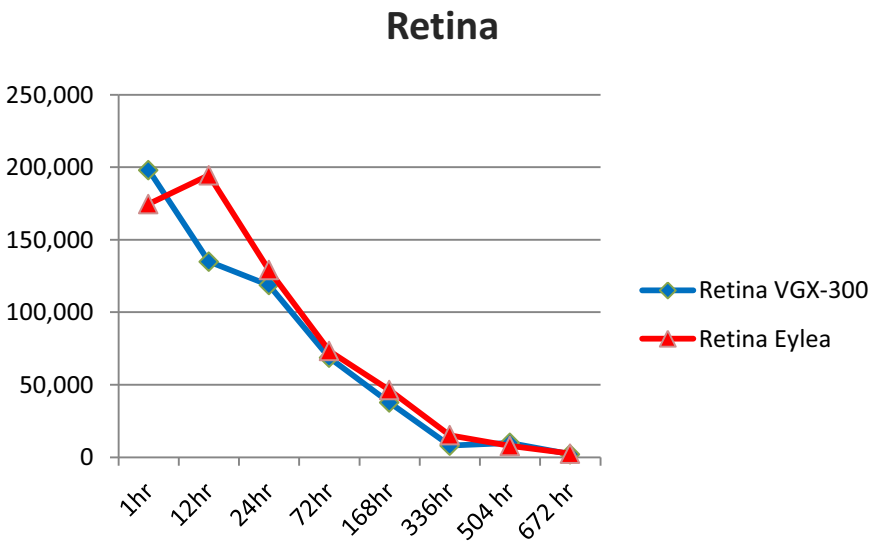


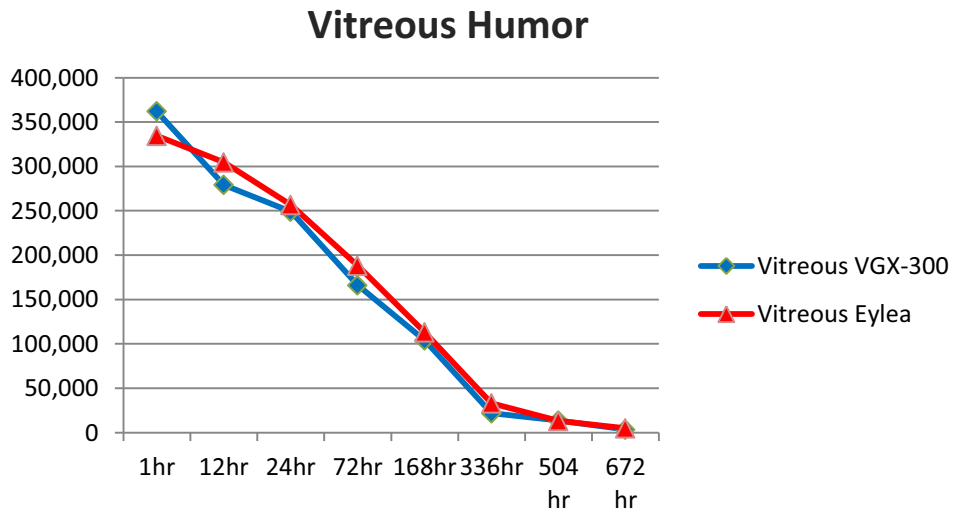
Elevated VEGF-C and its receptors in wet AMD clinical specimens



The Ocular Biodistribution and PK of OPT-302 is Comparable to EYLEA® in Rabbits

- OPT-302 has comparable ocular biodistribution and PK profile in rabbits to marketed agents – potential for:
  - Reduced dosing frequency
  - Better patient compliance





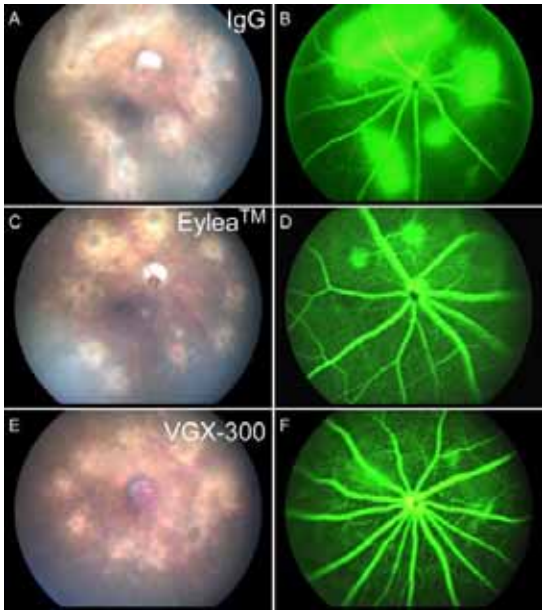
Concentration ngEq/mL

OPTHEA

Mouse Wet AMD model

Laser perforates Bruch's membrane

Vascular leakage of the retina (angiography and flourescent tracer – RHS)



- *"The mouse model of laser-induced choroidal neovascularization (CNV) has been used extensively in studies of AMD … and has served as the backbone for testing anti-antigenic therapies"* … Lambert *et al*. (2013)

OPTHEA

Lambert et al., Nature Protocols, 2013. Lashkari et al , 2013 ARVO Annual Meeting, 4999-A0128.

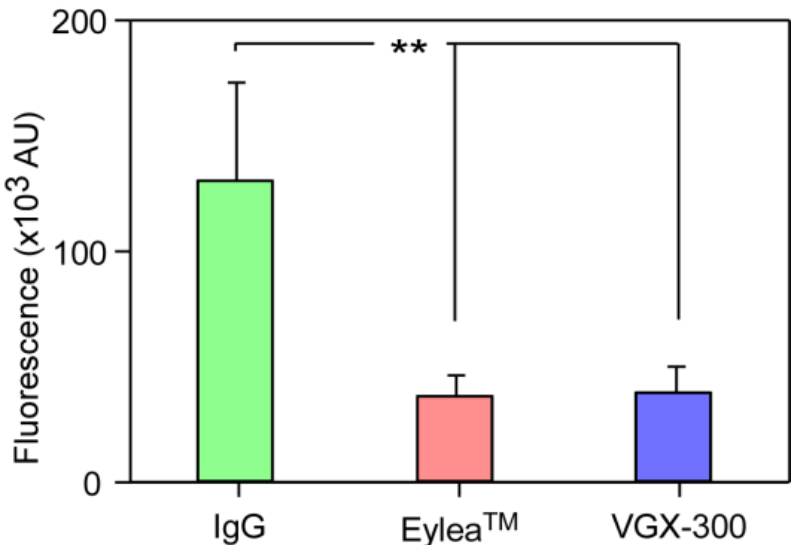
Mouse Wet AMD model

- In a mouse model of Wet AMD, VGX-300 has:
  - comparable efficacy to Eylea®
  - **additive** benefits when combined with Eylea®
- The pre-clinical data using VGX-300 has been compared to the pre-clinical data for Ophthotech's Fovista® compound (about to undertake a Phase 3 trial, Sept '13 IPO, Mkt cap >800M)

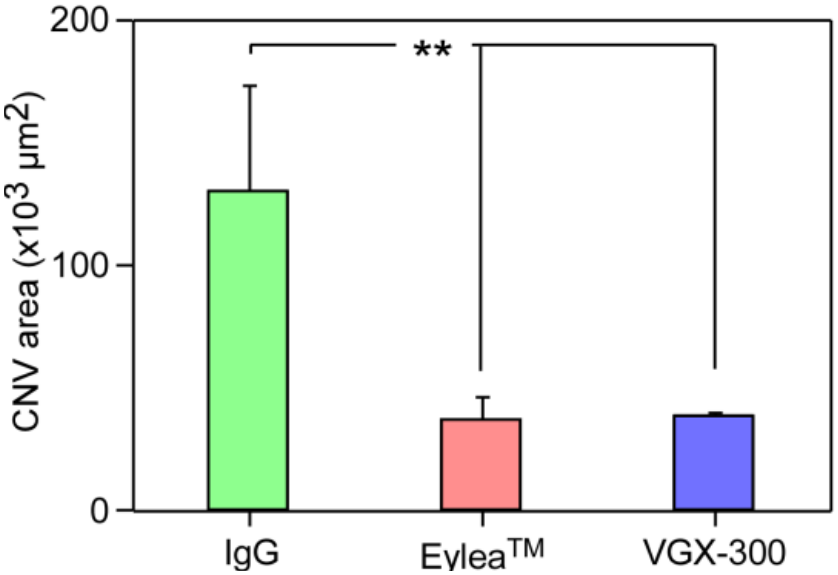
OPTHEA

Comparable activity of VGX-300 & Eylea® in mouse AMD

Reduction of vascular leakage in mouse CNV model



Reduction of CNV lesion area in mouse CNV model



Lashkari et al , 2013 ARVO Annual Meeting, 4999-A0128.
Schepens Eye Research Institute, Department of Opthamology, Harvard Medical School

OPTHEA

Ophthotech: Capital Raising and IPO
Significant implications for Opthea valuation

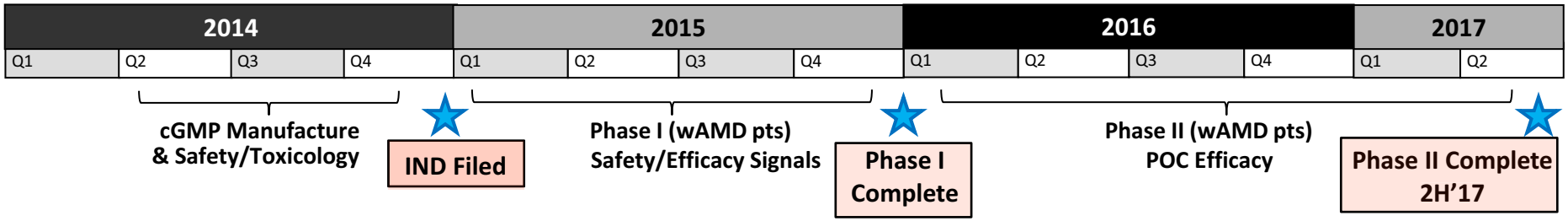
- Developing Fovista® (a-PDGF-b aptamer) as combination with a-VEGF-A therapy
  - Similar approach as Opthea to combine with existing a-VEGF-A therapies
- Published preclinical data 2006
- Fovista ® is not active as a single-agent in wet AMD; VGX-300 highly active as a single-agent in preclinical model

- Ophthotech Series A private funding round
  - $36M (2007) on basis of preclinical data
- Series B: $175M (May 2013)
- Completion of Phase 2b announced Oct 2012
- IPO (Sept 2013)
  - 7.6M shares @ $22 per share
  - Raised $167.2M
  - Trading at $26 - $34 per share
  - Current Mkt Cap >$800M

OPTHEA

Key Milestones

Our Phase I is designed to have meaningful efficacy measures



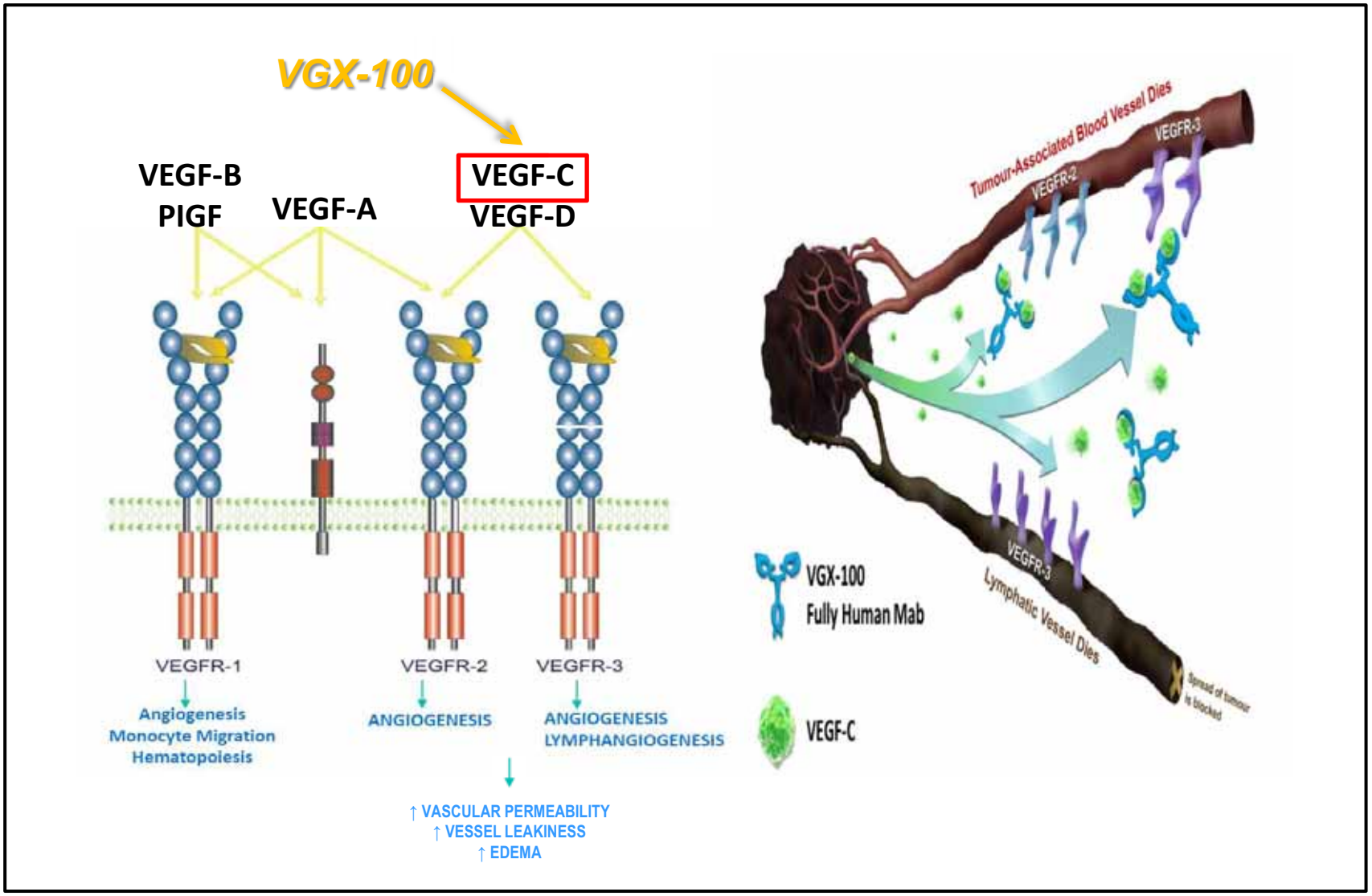
- **Initiating Phase I clinical study H1 CY2015**
  - Phase I safety/efficacy data within 2 years from now
  - Phase II clinical proof of principle within 3.5 years from now

Thank You!

www.opthea.com

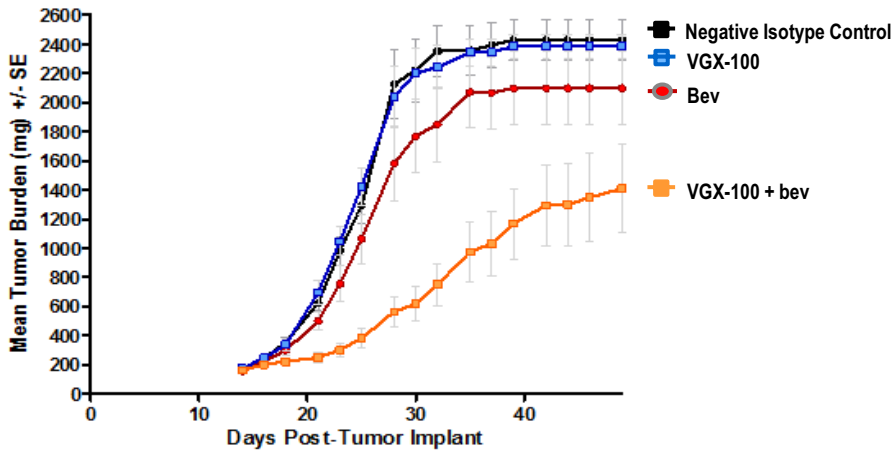
OPTHEA

VEGF-C Inhibition starves tumours & inhibits tumour spread

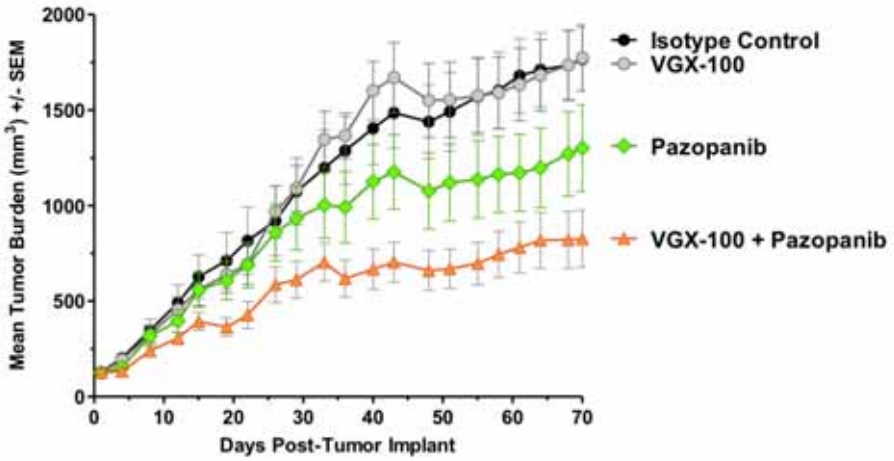


VGX-100 is effective in a wide range murine models of cancer: Alone or in combination with anti-angiogenic agents

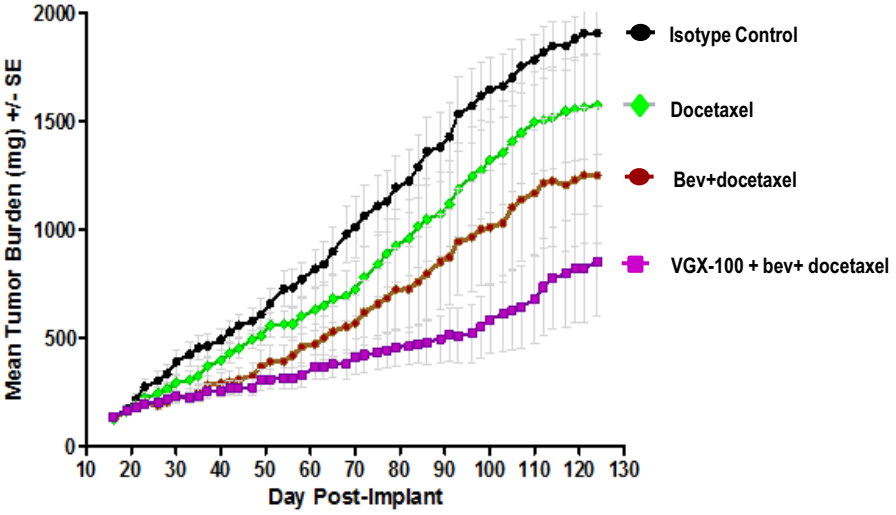
U87MG Glioblastoma



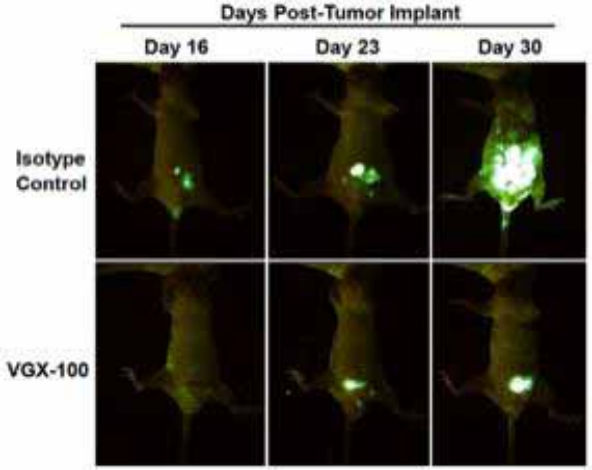
Colo205 Colorectal



OVCAR-8 Ovarian Cancer

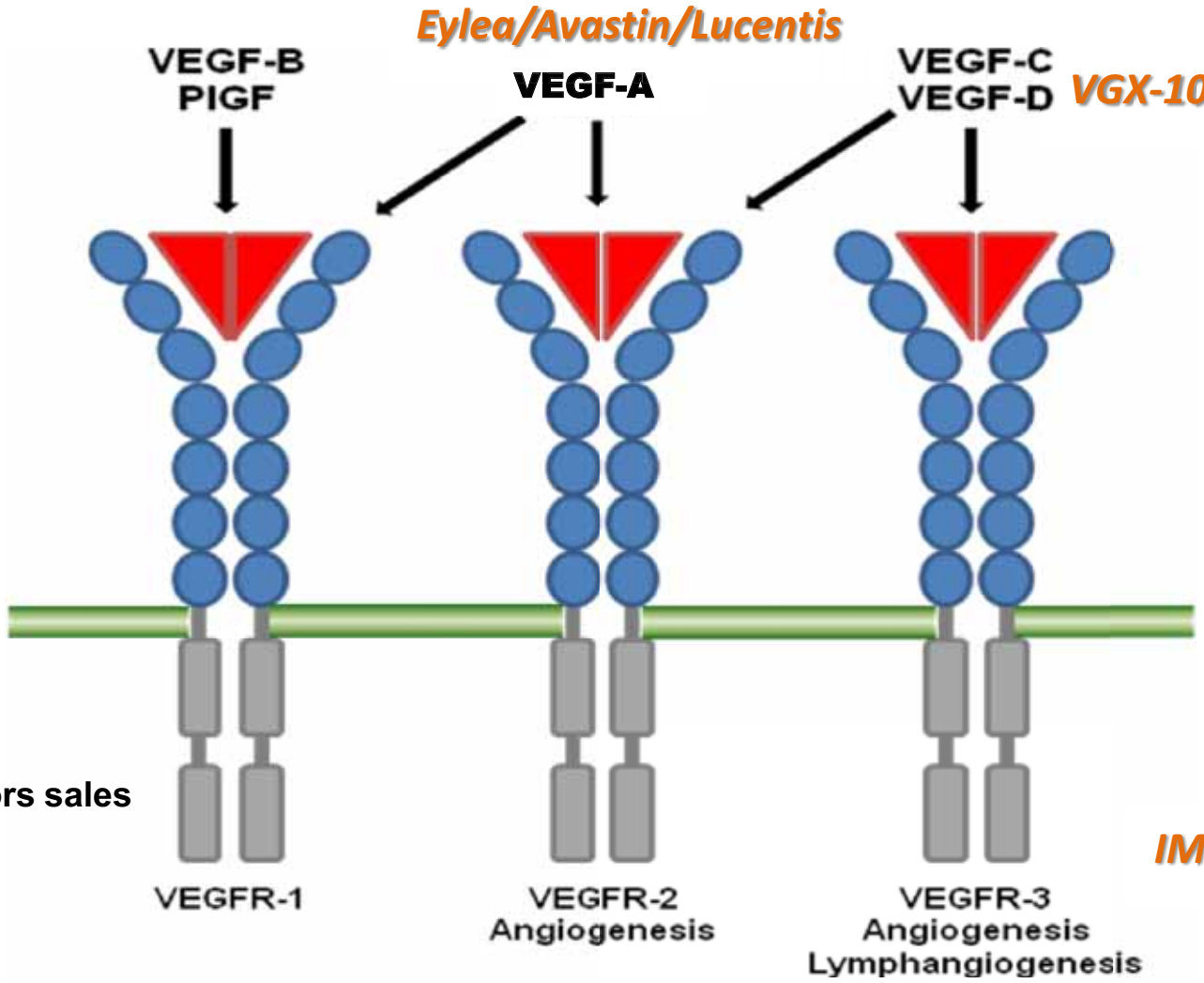


Metastatic PC3 prostate cancer model



THE VEGF PATHWAY IS NOT JUST VEGF-A

OUR IP COVERS OTHER MAJOR MOLECULES



VEGF-A inhibitors sales >$10B in 2012