Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY)

Corporate Presentation

September 2011

Robert Klupacs, CEO & Managing Director

circadian

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CORPORATE SNAPSHOT

Developer of biological therapies targeted to block angiogenesis AND lymphangiogenesis to treat cancer and eye disease

- Novel Vascular Endothelial Growth Factors (VEGF) antibody therapy based on tumor starvation and metastasis inhibition
- Anti-VEGF therapy has gained wide acceptance on the strength of Genentech/Roche Avastin® with 2010 US Sales of $7.2 billion
- A major opportunity to be used in combination with Avastin® and/or other anti-angiogenic therapies to improve patient outcomes in oncology or as a single agent in eye disease.

CORPORATE SNAPSHOT

Lead Internal Therapeutics program: VGX-100

Fully human, high affinity, neutralizing monoclonal antibody for VEGF-C

- Pre-clinical data demonstrating anti-tumourigenic and anti-metastatic effects in animal models of human prostate, pancreatic, brain, lung and ovarian cancers presented at AACR
- VEGF-C may be a predictive biomarker of Avastin® resistance in CRC – ASCO 2011

IND Filing Q4 2011

- Glioblastoma and mCRC first indications
- Expanding development to also include treatment of front-of-eye-diseases

CORPORATE SNAPSHOT

Partnered programs with existing and increasing royalty streams

Therapeutics: *VEGFR-3 antibody (IMC-3C5) for solid tumours*

- Development agreement with ImClone/Eli Lilly
- FDA Phase I trial started April 2011
- Annual Fees, Royalty on Sales

Diagnostics: *Cancer of Unknown Primaries (CUP) molecular diagnostic*

- Development partnership with Healthscope
- Launch in Asia expected H2 2011

Diagnostics: *VEGF-D diagnostic for respiratory diseases*

- Development partnership with Cincinnati Children's Hospital Medical Center;
- Launched Feb 11

CORPORATE SNAPSHOT

Dominant and protected IP position extending till at least 2025

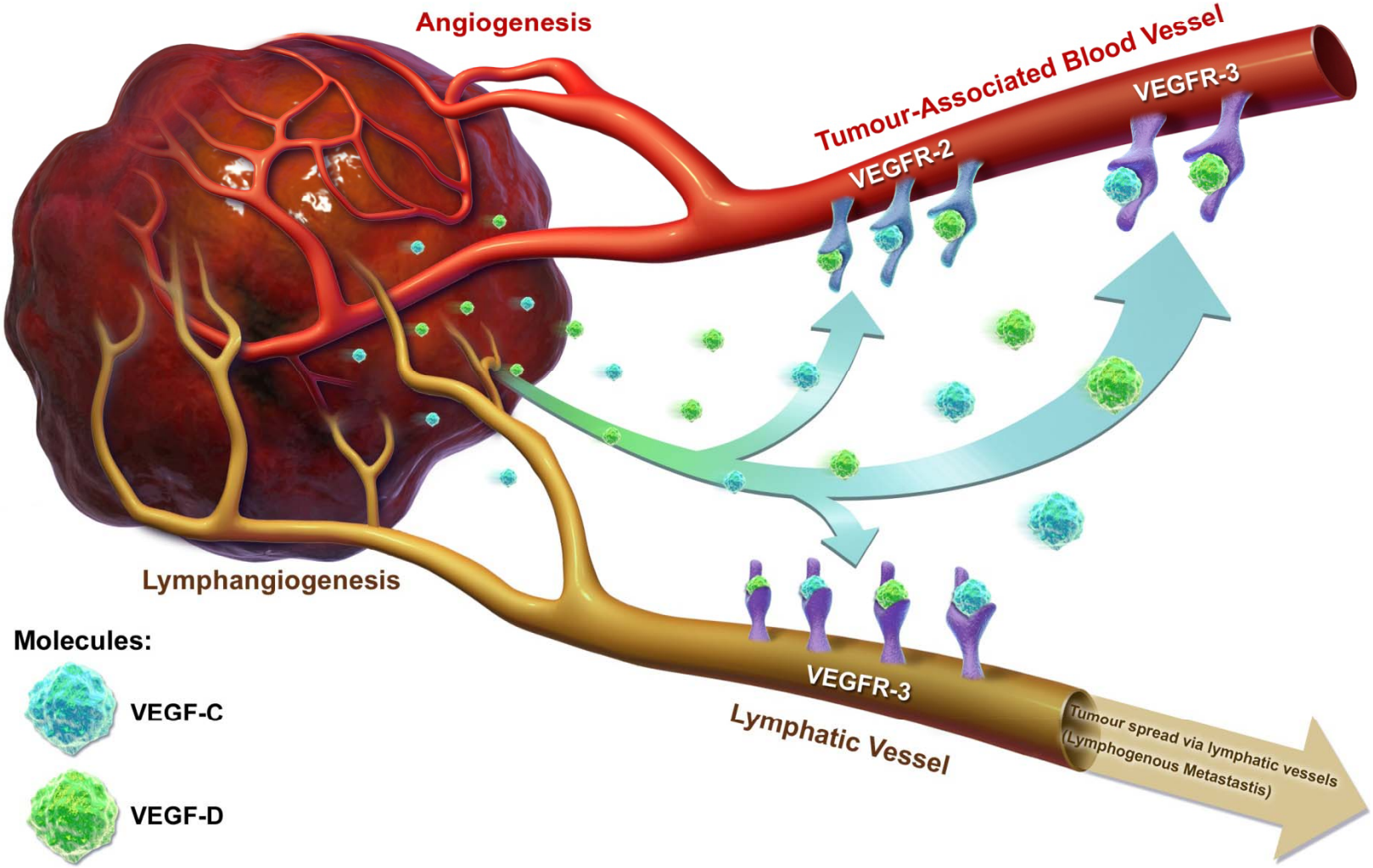
- Acquired from Ludwig Institute/Uni Helsinki
- Exclusive worldwide licences for VEGF-C –HGS/Cogenesys/Teva
- Exclusive worldwide licences for VEGF-D - Chugai (Jan 2011)

Strong financial position

- Approx $A22M cash and investments
- Cash Burn 2011/12 (est) $10-12.5M

VGX-100
VEGF-C Inhibition: Rationale

Mechanism of Circadian's Drugs: VGX-100 inhibits VEGF-C



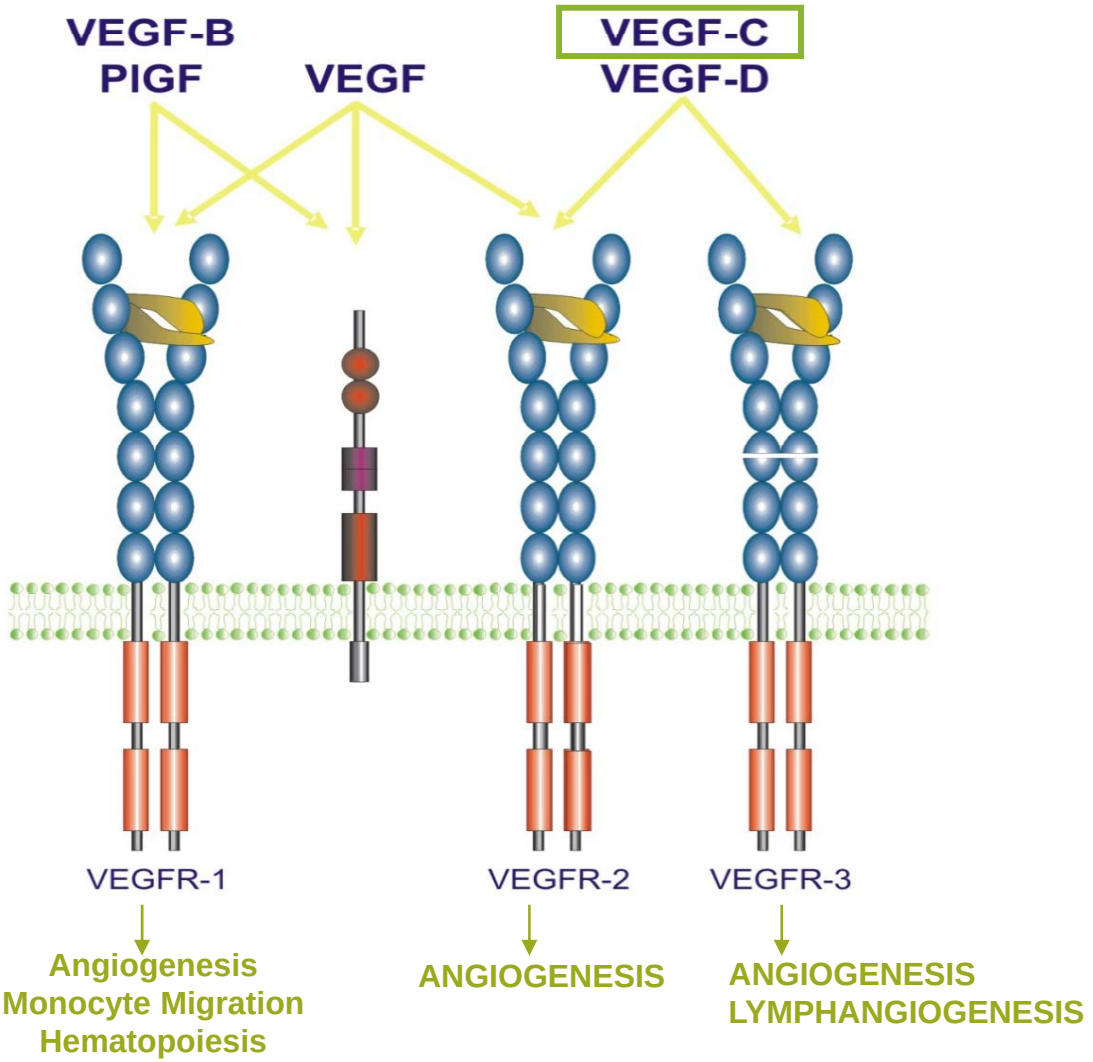
Our approach is based on the widely accepted view that combination targeted therapies is the way of the future in oncology

Since most tumors eventually find a way to get around blocked pathways,

"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.

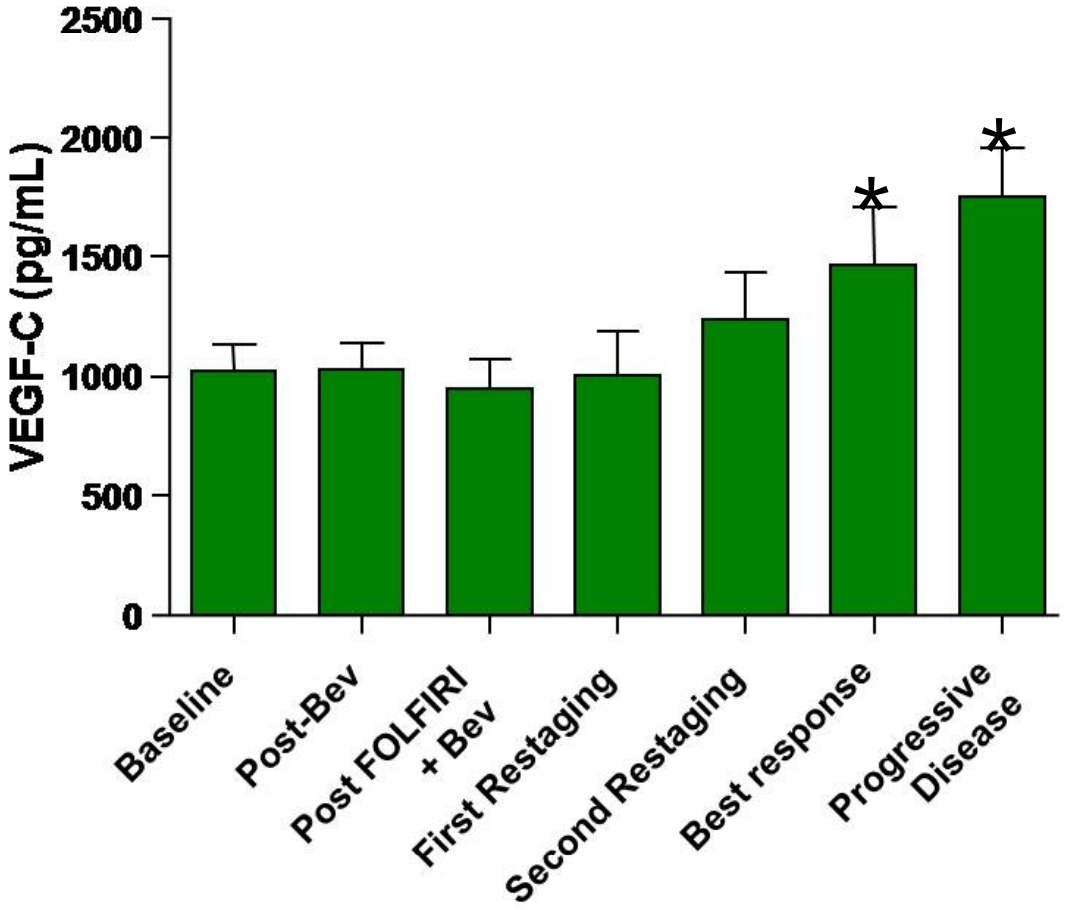
VEGF-C is a member of the VEGF family that binds VEGFR-2 and VEGFR-3



VEGF-C IN AVASTIN® 'ESCAPE'

- Avastin®: 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
  - Likely reasons:
    - Tumor growth due to factors other than VEGF; and/or
    - Other angiogenic factors being turned on when VEGF blocked (eg. VEGF-C)
- VEGF-C is a likely candidate mediating the tumoral growth 'escape' in anti-VEGF -resistant tumors.
- Upregulation of VEGF-C could maintain signalling through VEGFR-2, despite VEGF inhibition.

Circulating VEGF-C levels are elevated in Avastin®/FOLFIRI treated patients prior to disease progression



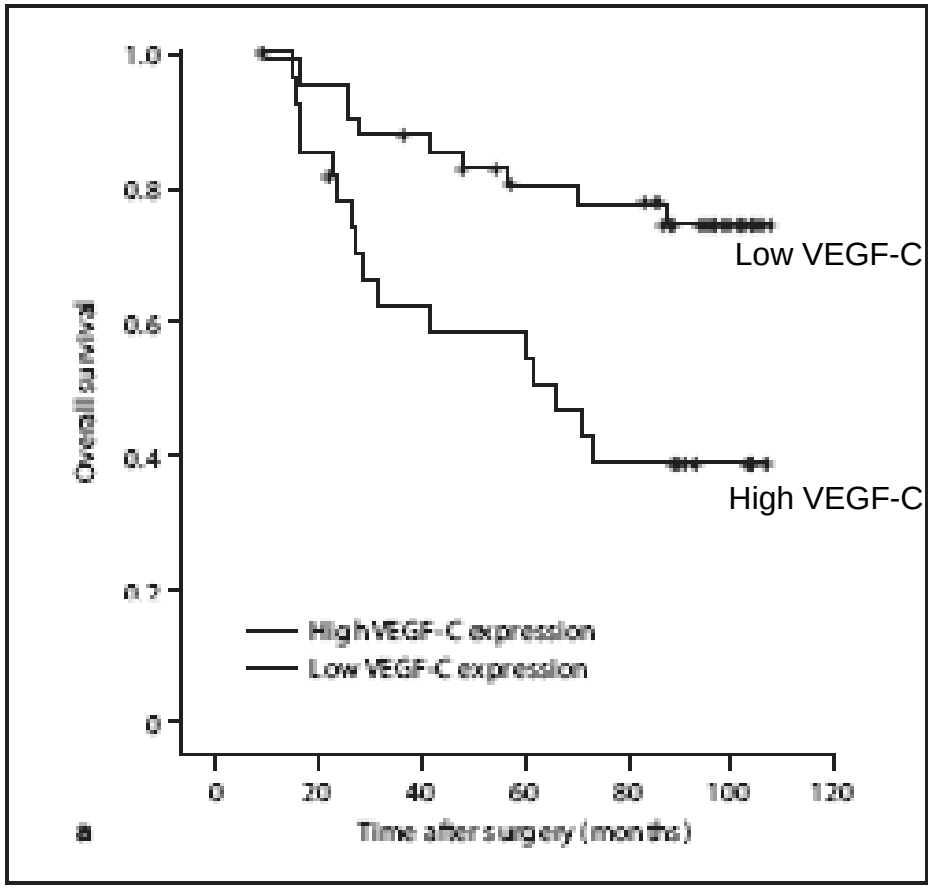
Plasma VEGF-C may be a predictive biomarker for the development of resistance to Bevacizumab

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 –well recognised survival prognostic factor in a number of tumour types

Some examples

VEGF-C is a risk factor for colorectal cancer



69 CRC

VEGF-C correlated with:

- LN Metastases
- Clinical Stage

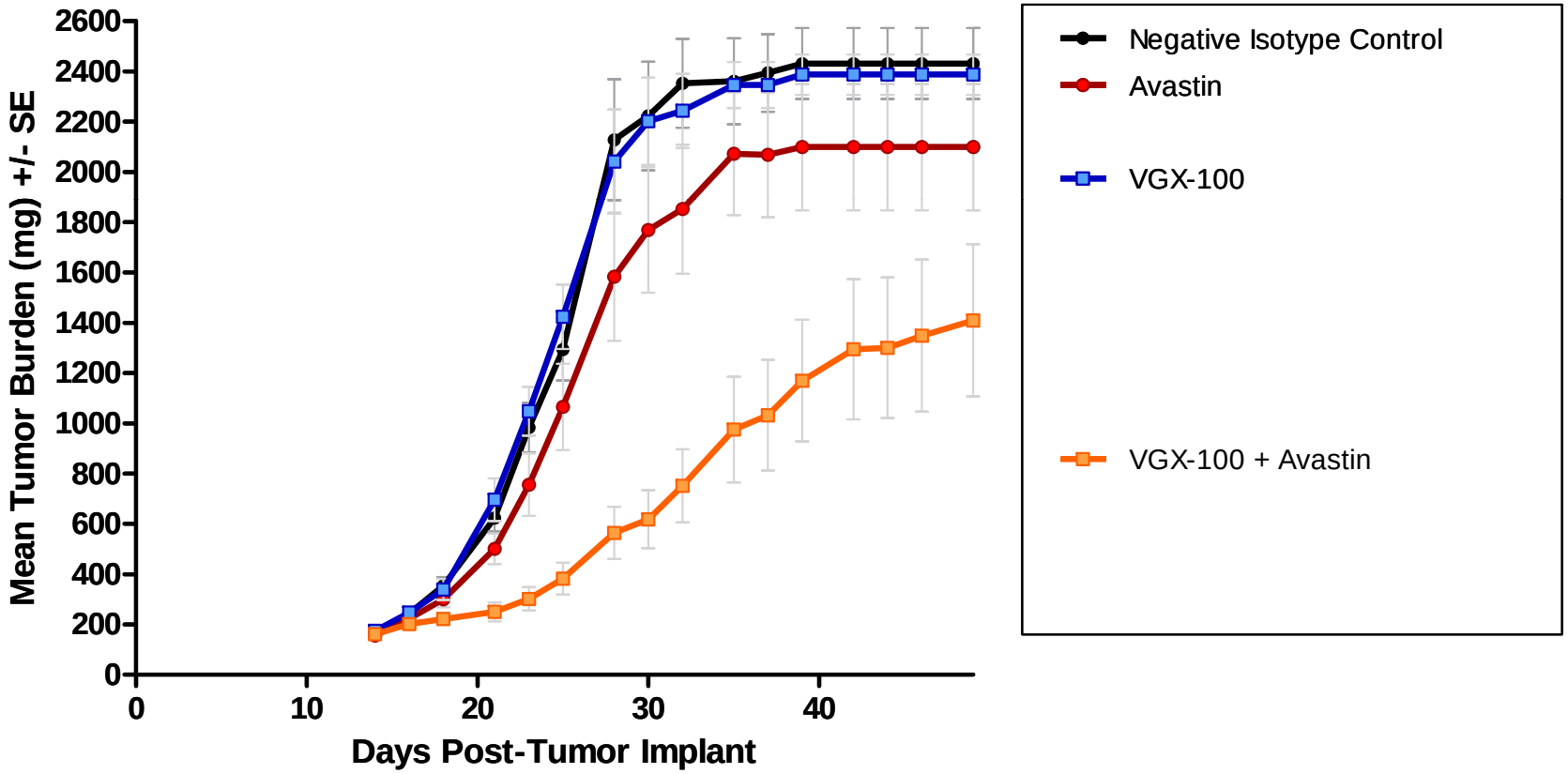
Elevated VEGF-C associated with:

- Decreased DFS
- Decreased OS

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

VGX-100 Efficacy in Mouse Models of Human Cancer

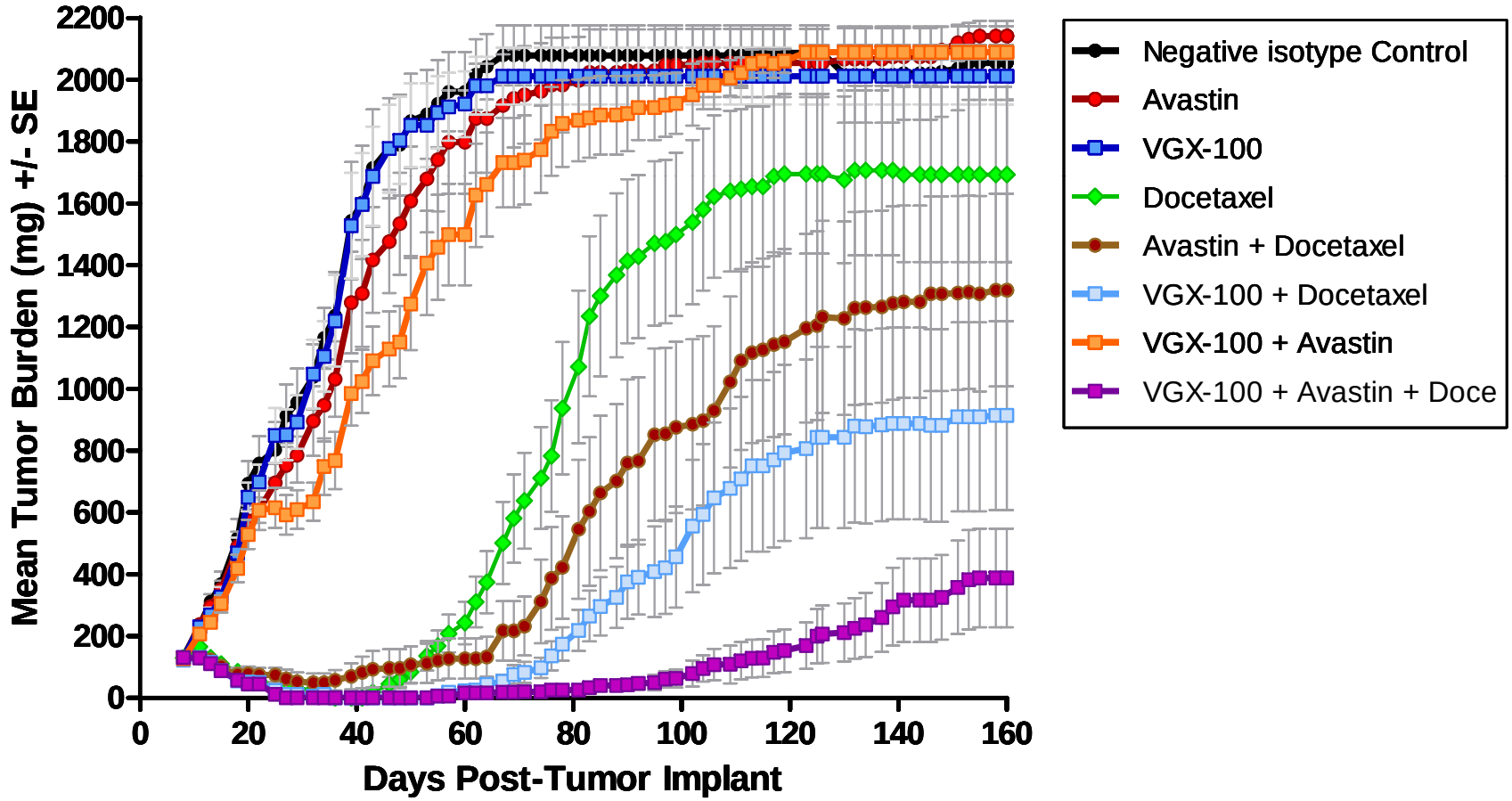
U87MG Glioblastoma Tumor Xenografts: VGX-100 effective in combination with Avastin



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

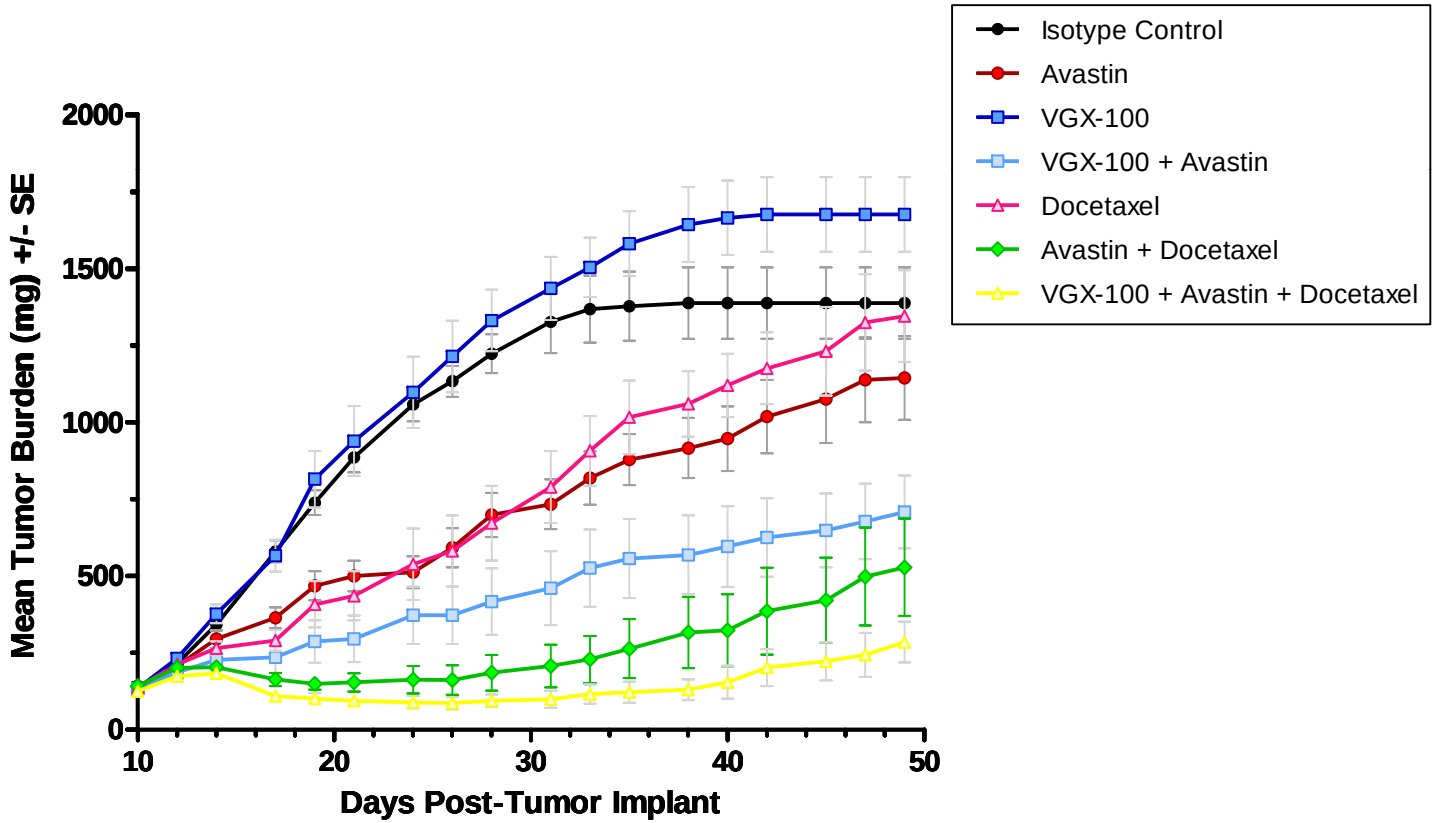
- 42% compared to control IgG
- 33% compared to single-agent Avastin.

VGX-100 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.

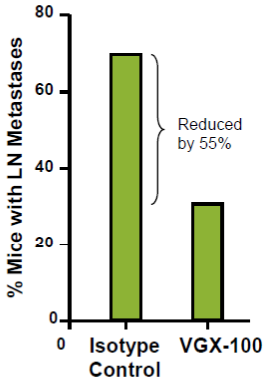
H292 NSCLC Tumor Xenografts: VGX-100 effective in combination with Avastin

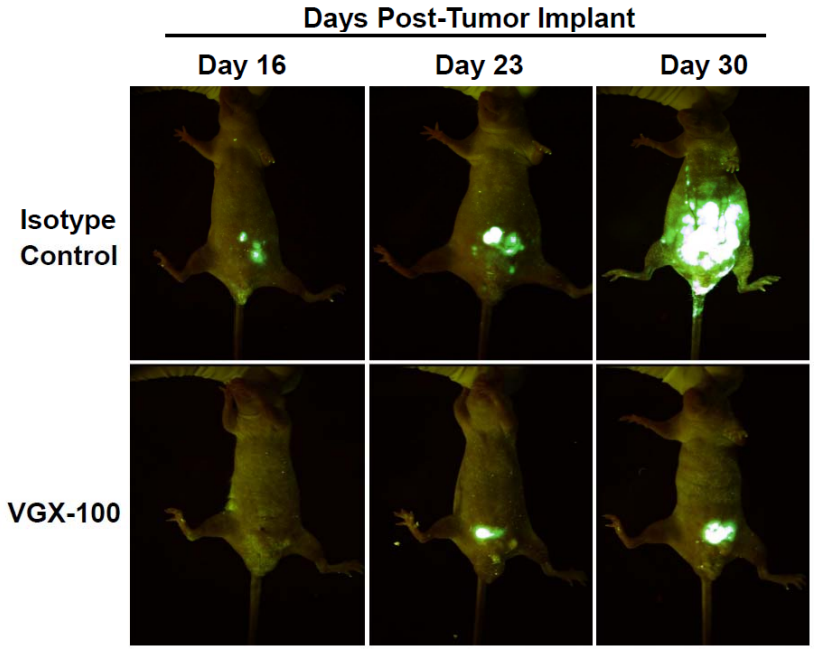


VGX-100 reduces metastasis in an orthotopic prostate cancer model

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.*





VGX-100 ONCOLOGY CLINICAL DEVELOPMENT

VGX-100 Target Product Profile in Oncology

- **Indication:**
  - Co-administered with anti-angiogenic agent (Avastin®) and standard of care
    - » Targeting glioblastoma, colorectal cancer
    - » At least one of breast, lung, renal and/or potentially ovarian cancer in combination with Avastin®
- **Optimal timing of treatment**
  - First line with Avastin®
  - In the treatment of Avastin® resistance
  - Phase I trials expected to commence in USA Q4 2011

Oncology Milestones Achieved to Date

- Extensive proof of concept studies in animal models
- GMP manufacturing process & drug product
  - Yield > 2g/L
  - Stable formulation
  - Clinical trial drug made
- GLP toxicology studies in two species completed
  - Safe & well-tolerated
- Pre-IND with FDA successful
- Phase I trial sites selected
- Phase 2 indications – Glioblastoma, Colorectal cancer

Glioblastoma

- In the US in 2010[1]
  - Estimated diagnosed: 22,020
  - Estimated fatalities: 13,140
- The most aggressive malignant primary brain tumor in adults
- Nearly always fatal
- Pre-Avastin®
  - 6-month progression-free survival for relapsed or progressive glioblastoma is 9% to 21%
  - objective response rate is less than 10%
  - median overall survival (OS) is 7 months or less
- With Avastin®
  - Median OS: 9.2 months

[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.

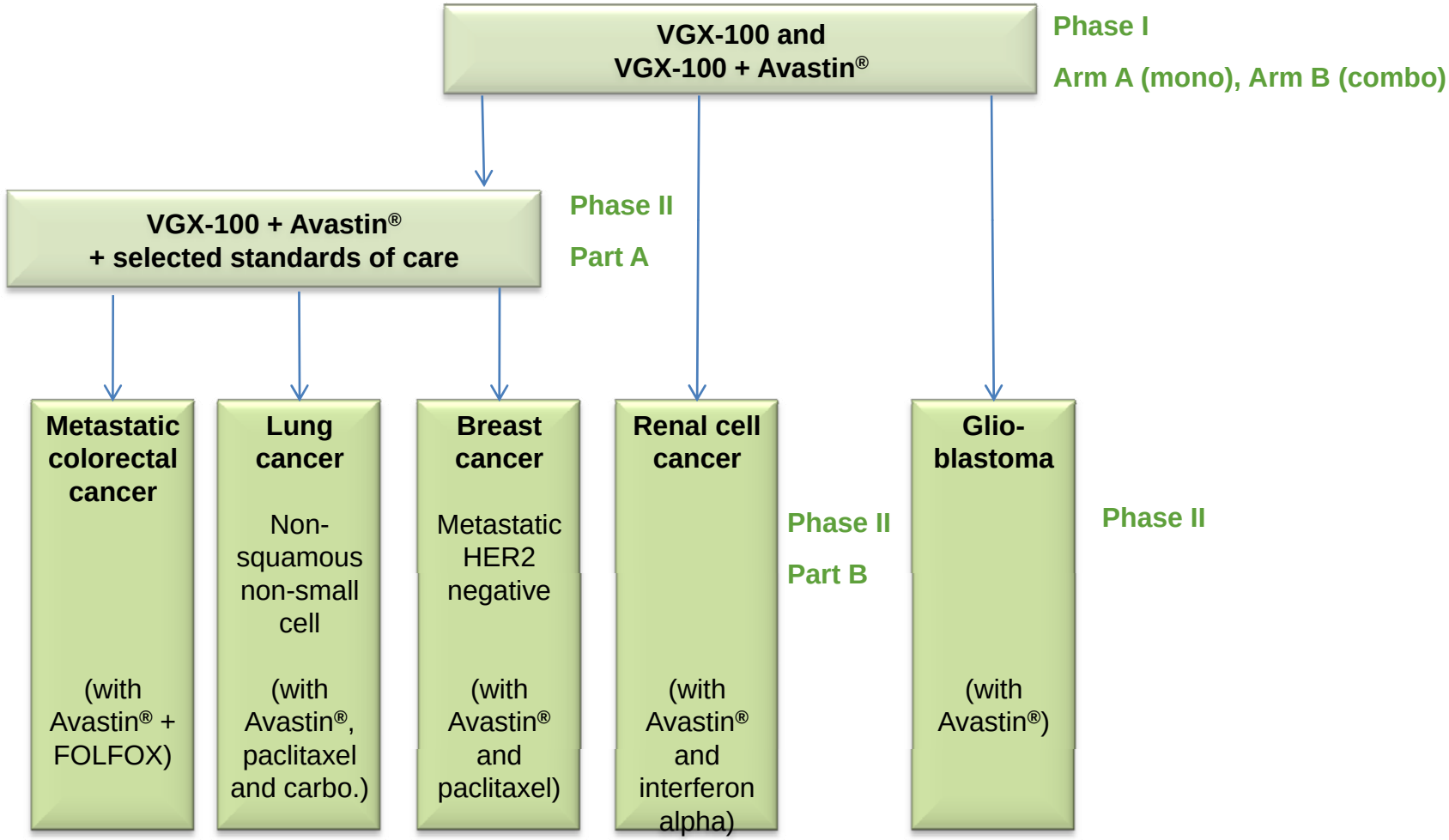
Metastatic colorectal cancer

- In the US[1]
  - 2nd most common cause of cancer deaths[2]
  - Estimated diagnosed in 2010: 142,570
  - Estimated fatalities in 2010: 51,370
- At presentation (% 5-year relative survival):
  - 39% localized (90%)
  - 37% regional (68%)
  - 19% distant (10%)
- The median OS with Avastin®: 20.3 months

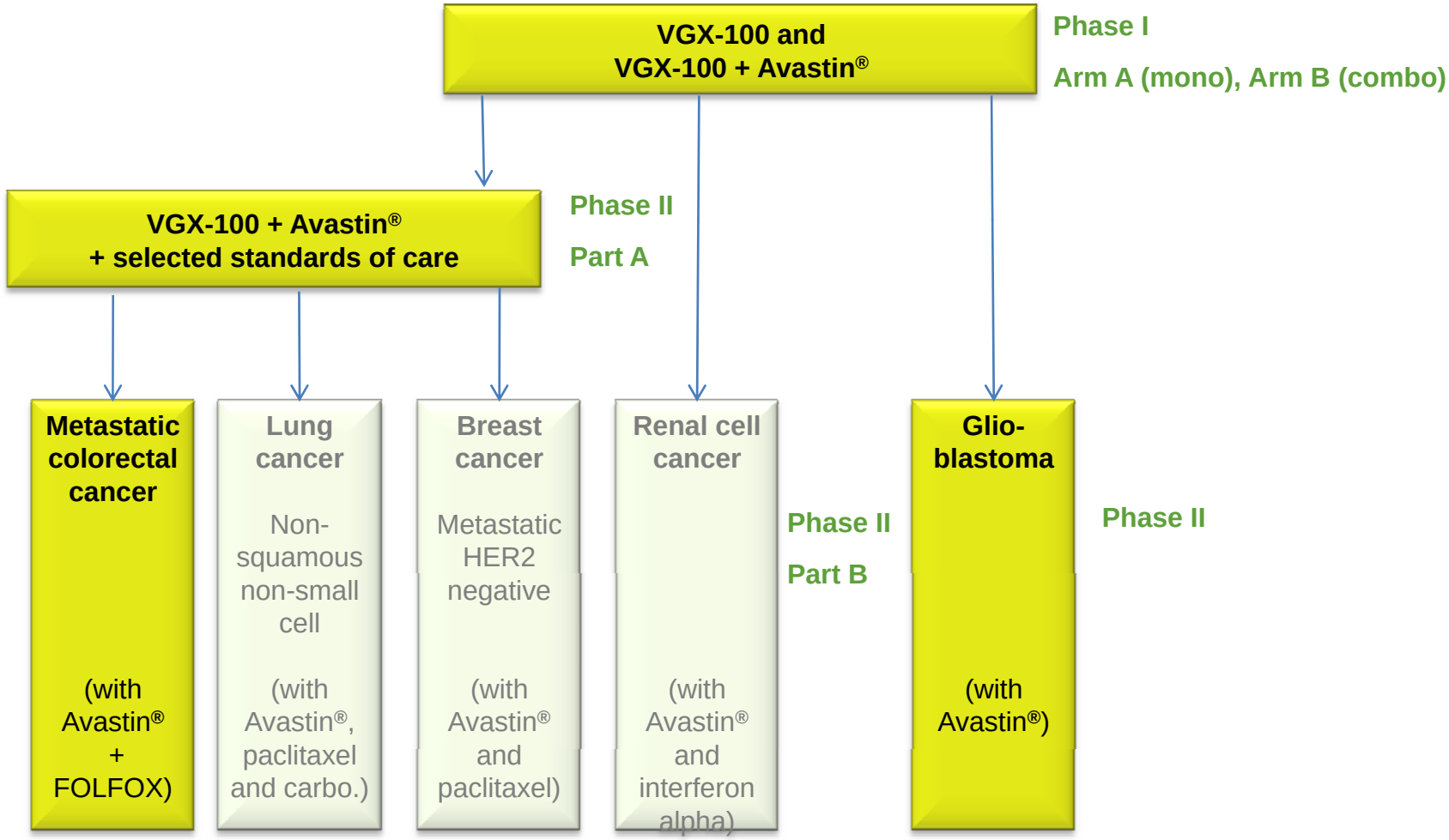
[1] *Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2008, National Cancer Institute. seer.cancer.gov/csr/1975_2008/ based on November 2010 SEER data submission, posted to the SEER web site, 2011.*

[2] *Kim G, Grothey A. Treatment Trends in Colorectal Cancer. Business Briefing: US Gastroenterology Review. 2005*

Phase I and II clinical program



Phase I and II clinical program



Avastin® Registrational Study in Glioblastoma

VOLUME 27 · NUMBER 28 · OCTOBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Bevacizumab Alone and in Combination With Irinotecan in Recurrent Glioblastoma

Henry S. Friedman, Michael D. Prados, Patrick Y. Wen, Tom Mikkelsen, David Schiff, Lauren E. Abrey, W.K. Alfred Yung, Nina Paleologos, Martin K. Nicholas, Randy Jensen, James Vredenburgh, Jane Huang, Maoxia Zheng, and Timothy Cloughesy

From the Brain Tumor Center, Duke University, Durham, NC; Department of Neurosurgery, University of California, San Francisco, San Francisco; Genetech Inc, South San Francisco; and Department of Neurology, University of California, Los Angeles School of Medicine, Los Angeles, CA; Department of Neurology, Brigham and Women's Hospital and Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston, MA; Hermelin Brain Tumor Center, Henry Ford Hospital, Detroit, MI; Department of Neurology, University of Virginia, Charlottesville, VA; Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY; Department of Neuro-Oncology, M. D. Anderson Cancer Center, Houston, TX; Division of Neurology, Evanston Northwestern Healthcare, Evanston, IL; Department of Neurology,

A B S T R A C T

Purpose

We evaluated the efficacy of bevacizumab, alone and in combination with irinotecan, in patients with recurrent glioblastoma in a phase II, multicenter, open-label, noncomparative trial.

Patients and Methods

One hundred sixty-seven patients were randomly assigned to receive bevacizumab 10 mg/kg alone or in combination with irinotecan 340 mg/m^2 or 125 mg/m^2 (with or without concomitant enzyme-inducing antiepileptic drugs, respectively) once every 2 weeks. Primary end points were 6-month progression-free survival and objective response rate, as determined by independent radiology review. Secondary end points included safety and overall survival.

Results

In the bevacizumab-alone and the bevacizumab-plus-irinotecan groups, estimated 6-month progression-free survival rates were 42.6% and 50.3%, respectively; objective response rates were 28.2% and 37.8%, respectively; and median overall survival times were 9.2 months and 8.7 months, respectively. There was a trend for patients who were taking corticosteroids at baseline to take stable or decreasing doses over time. Of the patients treated with bevacizumab alone or

Current Activities and Value Adding Events

Activity	Timeline
Mechanism of Action Studies	Complete
PK Studies	Complete
cGMP Manufacture	Complete
Toxicology Studies	Complete
IND Filing	Q4 2011
First-in-human Clinical Study Initiation (monotherapy and in combination)	Q4 2011
Phase I trial complete	Q4 2012
Phase II studies start (Multiple Indications)	Q1 2013
Clinical proof-of-concept in Glio (Basis for registration?)	2H 2014

VGX-100 OCULAR DEVELOPMENT OPPORTUNITY

Compelling Reasons Supporting Development of VGX-100 for Eye-Disease

- Opportunity to leverage VGX-100 oncology program
- Scientific rationale
- Existing supportive preclinical data
- Relationship with Key Opinion Leader
- Mechanism of Action differentiation from VEGF-A inhibitors
- Defined clinical endpoints using validated procedures
- Short timeframe to clinical POC
- Large market opportunity (>$1B p.a)

Development Opportunity

- Significant development opportunity for VGX-100 as a treatment for 'front of the eye' disease.

- Initial indications:
  - **Corneal Neovascularisation (CNV)**
    - Estimated that up to 4-5% of patients at eye clinics have CNV
  - **High-Risk Corneal Allograft Rejection**
    - >10000 grafts/yr in USA
  - **Dry Eye Disease**
    - Affects 5M people over 50 yrs in USA
    - 1 drug "Restasis" sells >$1B/yr worldwide
    - Preclinical POC data to be published Sept '11.

- Local ocular administration via subconjunctival injection as a single-agent.

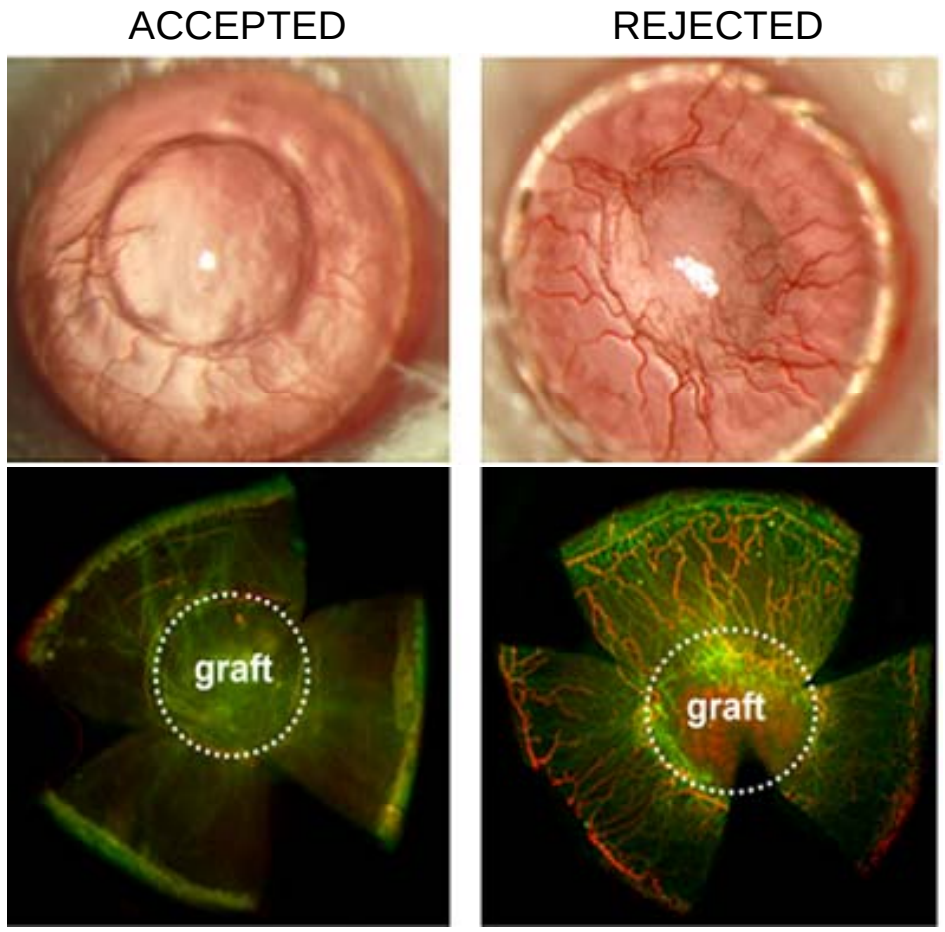
- Approx. 12 – 18 months to Phase I/II

Existing & Supportive Preclinical Data:

VGX-100 improves Corneal Transplant Survival

Rejected corneas are infiltrated by blood and lymphatic vessels and over-express VEGF-C and VEGFR-3

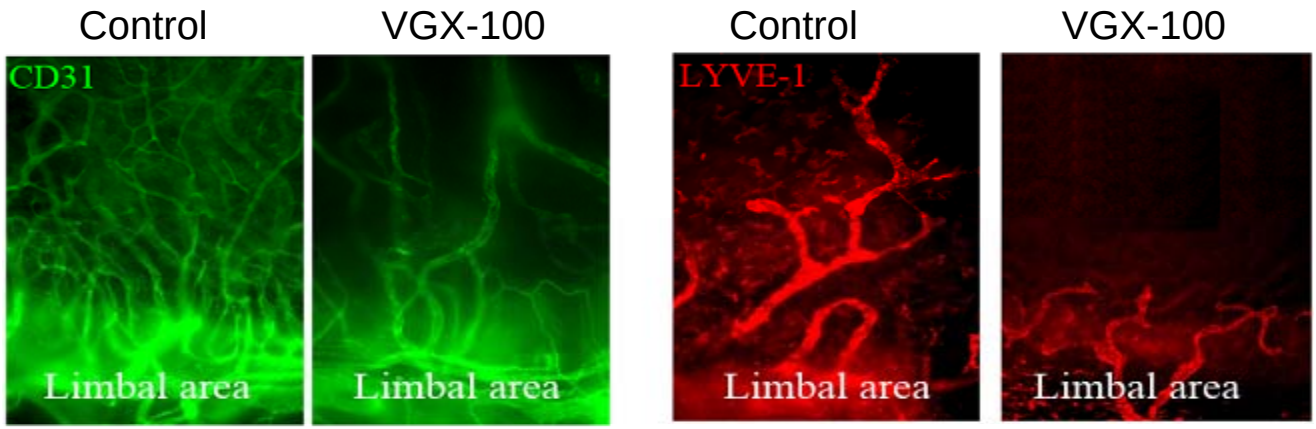
Transplanted Corneas: 3 wks Post-Transplant

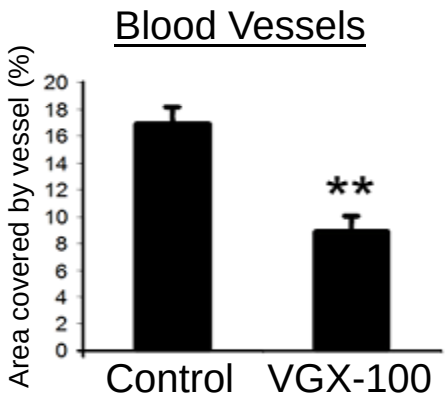


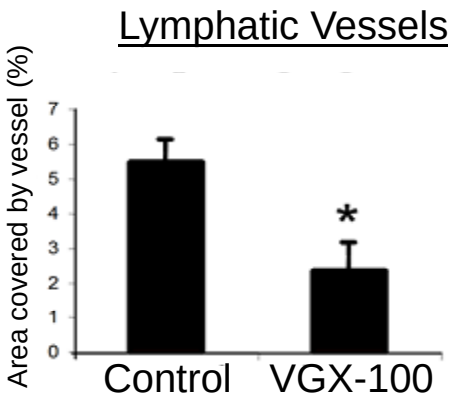
VEGF-C expression increased 2-fold in rejected vs accepted allografts, and 4.8 fold over non-transplanted corneas.

ARVO Annual Meeting 2010. Program#/Poster#1554/D995

VGX-100 reduces blood and lymphatic vessel density in transplanted corneas

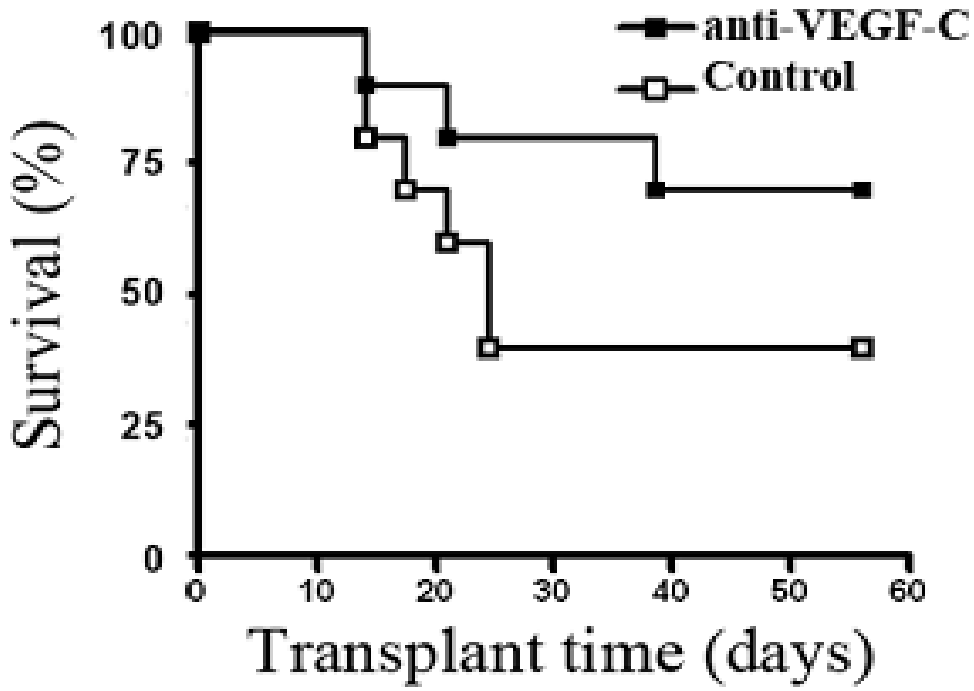






Day 7 post-transplant

VGX-100 Promotes Corneal Transplant Survival



ARVO Annual Meeting 2010. Program#/Poster#1554/D995

Current Activities and Value Adding Events

ACTIVITY	TIMELINE
Further efficacy data in preclinical CNV & Corneal Transplant & Dry Eye models	4Q'11 – 2H'12
Acceptable biodistribution and PK via subconjunctival injection	2H'12
Acceptable profile in toxicology program via subconjunctival route	2H'13
IND granted	2H'13
Phase I/11 study start	2H'13
Proof of Concept Efficacy	1H'15

Corporate Details

A strong financial position & shareholder base

Top 10 shareholders: 55.6%

Investor	% of issued shares
Packer and Co Limited	16.66
Licentia Ltd	6.79
Ludwig Institute for Cancer Research	6.73
Select Asset Management	5.10
Leon Serry	4.53
HSBC Custody Nominees (GSCo) (NY Fund)	3.45
Chemical Trustee Limited &assoc	3.36
HSBC Custody Nominees (NY Fund)	2.70
National Nominees	2.30
Citigroup Nominees	2.23
JFF Steven Pty Ltd	1.76
Total 10 shareholders own	**55.6%**
Total 20 shareholders own	**63.0%**

Financial Summary @ 30 August 2011 (unaudited)

Stock code:	**CIR**
Share price:	60c (AUD)
Shares issued + deferred issue:	46,396,928
Market cap:	~ A$27 mill
Cash holdings: Listed investments: (ASX: ANP, OIL)	~ A$21 mill A$2.0M

Cash Burn estimate 2011/12 $10-12m

Institutions/Funds: ~ 43%

Retail investors: ~ 30%

Professional investors: ~ 27%

Key Development Milestones

Activity	Timeline
CUP Test Launch	H2 2011
VGX-100 publication of results in dry eye disease	Q3 2011
VGX-100 IND Filing	**Q4 2011**
VGX-100 First-in-human cancer patients Clinical Study commenced	**Q4 2011**
VGX-100 & Avastin Phase 1 trials commenced	**Q2 2012**
VGX-100 Phase 1 studies completed	**H2 2012**
IMC-3C5 Phase 1 trials reported	**H1 2013**
Phase II studies in cancer patients start (Multiple Indications)	Q1 2013
VGX-100 IND Filing Front of Eye Disease	H2 2013
Clinical proof-of-concept in cancer	**2H 2014**

Key Reasons to Invest

- **Clinical Stage Assets**
  - One product in the clinic – IMC-3C5 being developed by Eli Lilly
  - VGX-100 by Q4 2011 in oncology
  - VGX-100 by Q1 2013 in eye disease
  - Major value adding clinical data from Q3 2012

- **Increasing Diagnostics Portfolio generating revenues**
  - VEGF-D diagnostic on the market for LAM in USA; other territories next 6-12 months
  - CUP test likely launch by Healthscope Q4 2011
  - VEGF-C and VEGF-D diagnostics in cancer currently in development

Key Reasons to Invest

- **A platform with major deal/partnering potential across a range of products over next 3-18 months**
  - VGX-100 in oncology
  - VGX-100 in eye disease
  - VEGF-C diagnostics in oncology
  - VEGF-D diagnostics in oncology
  - VEGF-C/D proteins in wound healing, cardiac disease, bone disease
- **Investments coming up to major re-rating events**
  - ANP ATL1103 clinical data
  - OIL culmination of “strategic review”

Key Reasons to Invest

- **Re-rating of Value imminent**
  - Trades at cash backing
  - Historical valuation based on LIC history
  - Significant mispricing compared to comparables in USA, Europe and Australia
  - Drivers: – clinical trial commencement and/or partnerships

- **Capability to get to key value adding events**
  - Approx $22M in cash and investments
  - Superb internal and external drug development teams

Thank You

www.circadian.com.au