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

Biopartnering Europe

October 10, 2011

Robert Klupacs, CEO & Managing Director

circadian

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CORPORATE SNAPSHOT

- **Major IP Platform covering VEGF-C, VEGF-D and VEGFR-3**

- **Developing unique antibody therapies - VGX-100**
  - As combination therapy in chemotherapy (P1 to commence Q4 '11)
  - As monotherapy in front of eye disease (P1 to commence Q4 '12/Q1 '13)
  - IMC-3C5 being developed by Eli Lilly/Imclone (P1 commenced Apr 11)

- **Developing Diagnostics as early stage revenue source**
  - From Platform
    - VEGF-D in respiratory disease and treatment monitoring
    - VEGF-C in oncology and monitoring Avastin therapy
  - Cancers of Unknown Primary – partnered with Healthscope

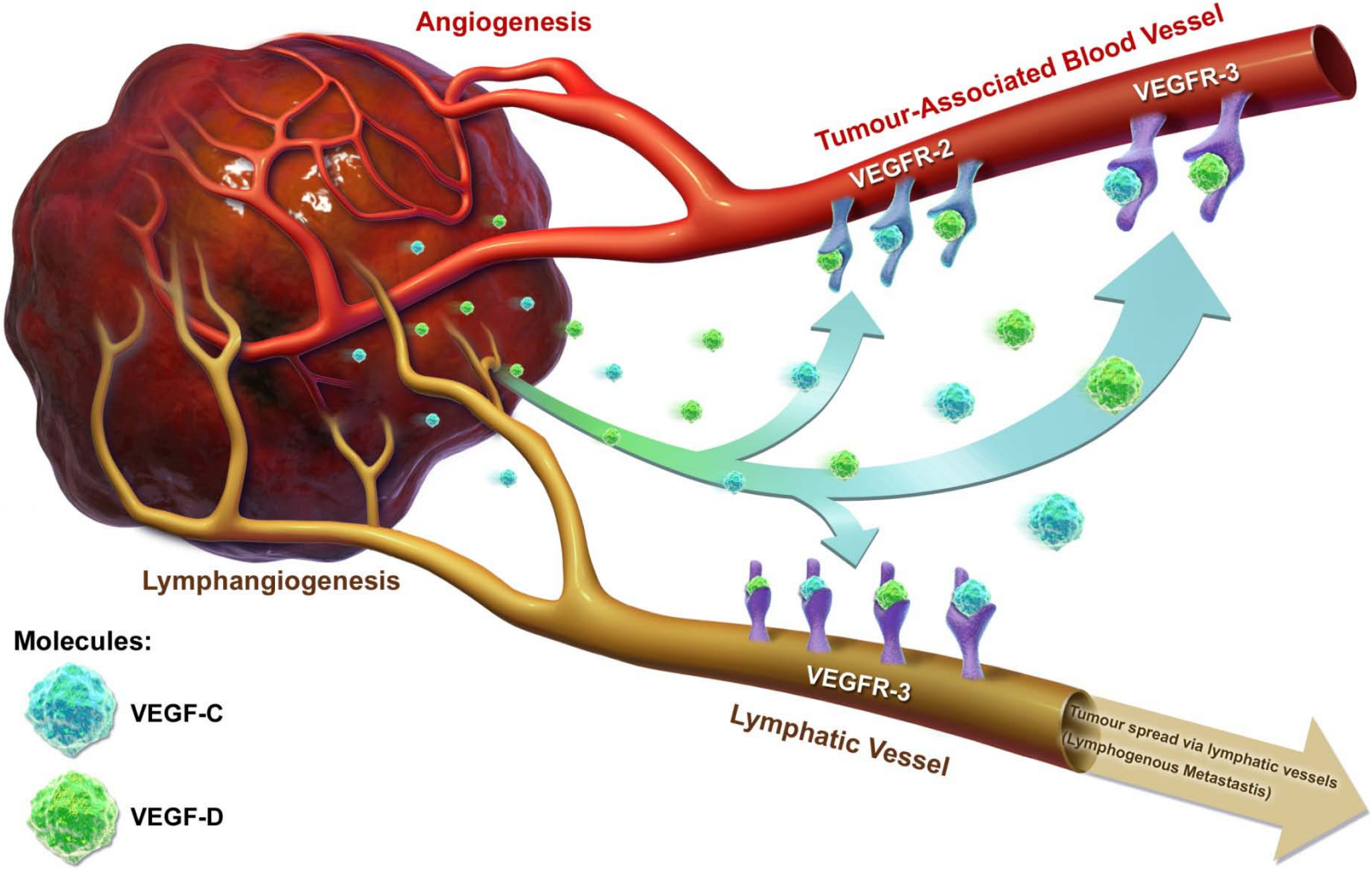
- **Additional Revenue generating partnerships**
  - Ark Therapeutics – VEGF-D gene therapy
  - R&D Systems Inc, Merck Millipore, Perkin Elmer – Research reagents

CORPORATE SNAPSHOT

Our antibodies are targeted to block angiogenesis AND lymphangiogenesis to treat cancer and eye disease

- Novel Vascular Endothelial Growth Factors (VEGF-C) 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
- Significant potential as monotherapy in front of the eye disease.

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



CORPORATE SNAPSHOT

Our Lead Internal Therapeutics program: VGX-100

- **Fully human 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 shown to be potential predictive biomarker of Avastin® resistance in Colorectal cancer – ASCO 2011
- **IND Filed September 30 2011**
- **Phase 1 multi-dose ascending trials to commence Q4 in cancer patients**
- **Glioblastoma and mCRC first indications**
  - Also 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

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

- Development partnership with Healthscope
- Launch in Asia expected H1 2012

Platform 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

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,

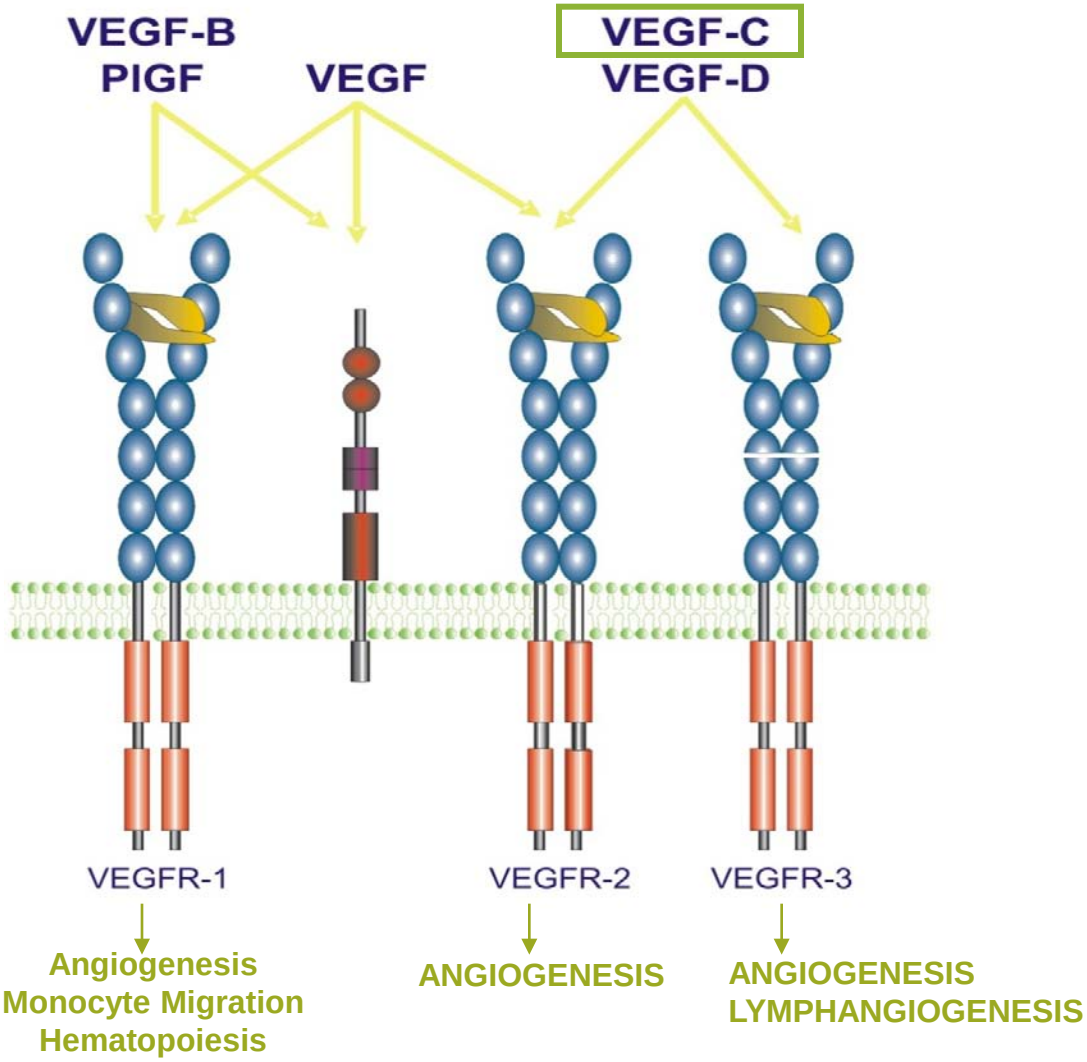
"there is widespread understanding that we are going to need to learn how to combine two or more targeted therapies to block the main road and the side road and the dirt road…"

ASCO Chief Executive Dr. Allen Lichter, ASCO Annual meeting June 2011.

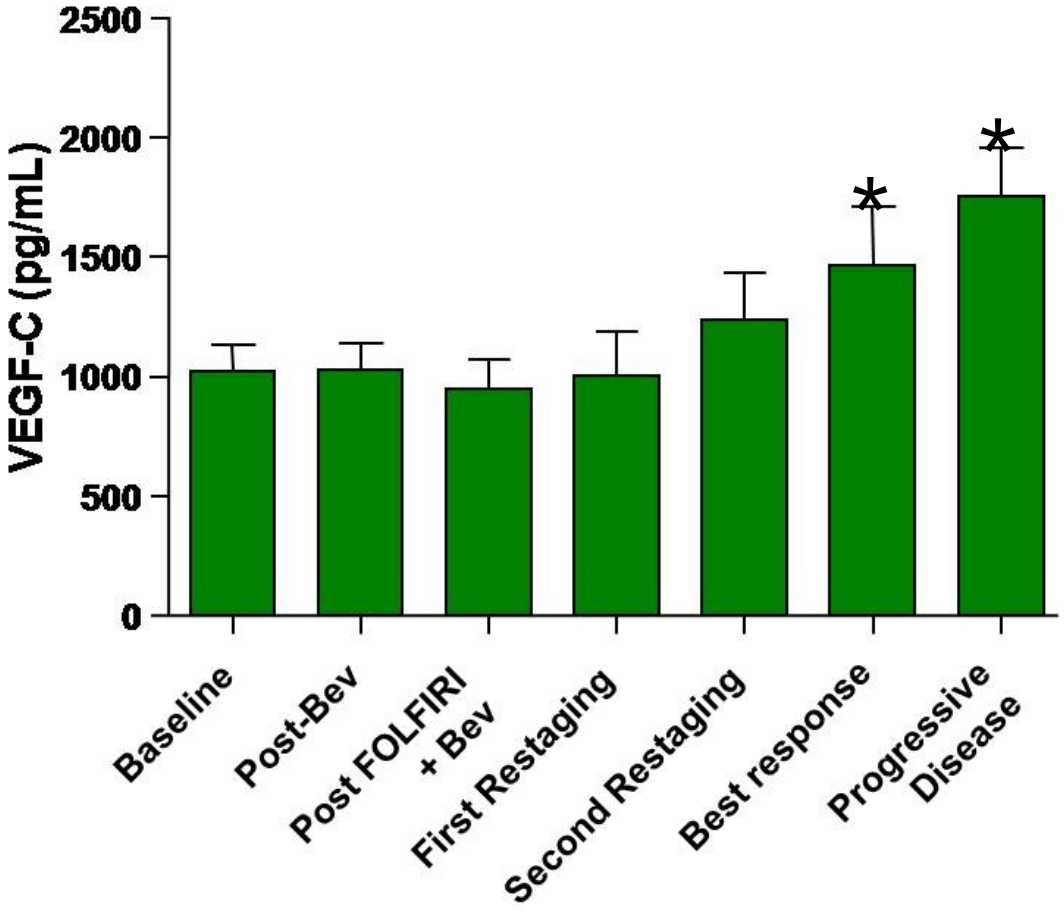
VEGF-C IN AVASTIN® 'ESCAPE'

- 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.

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



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

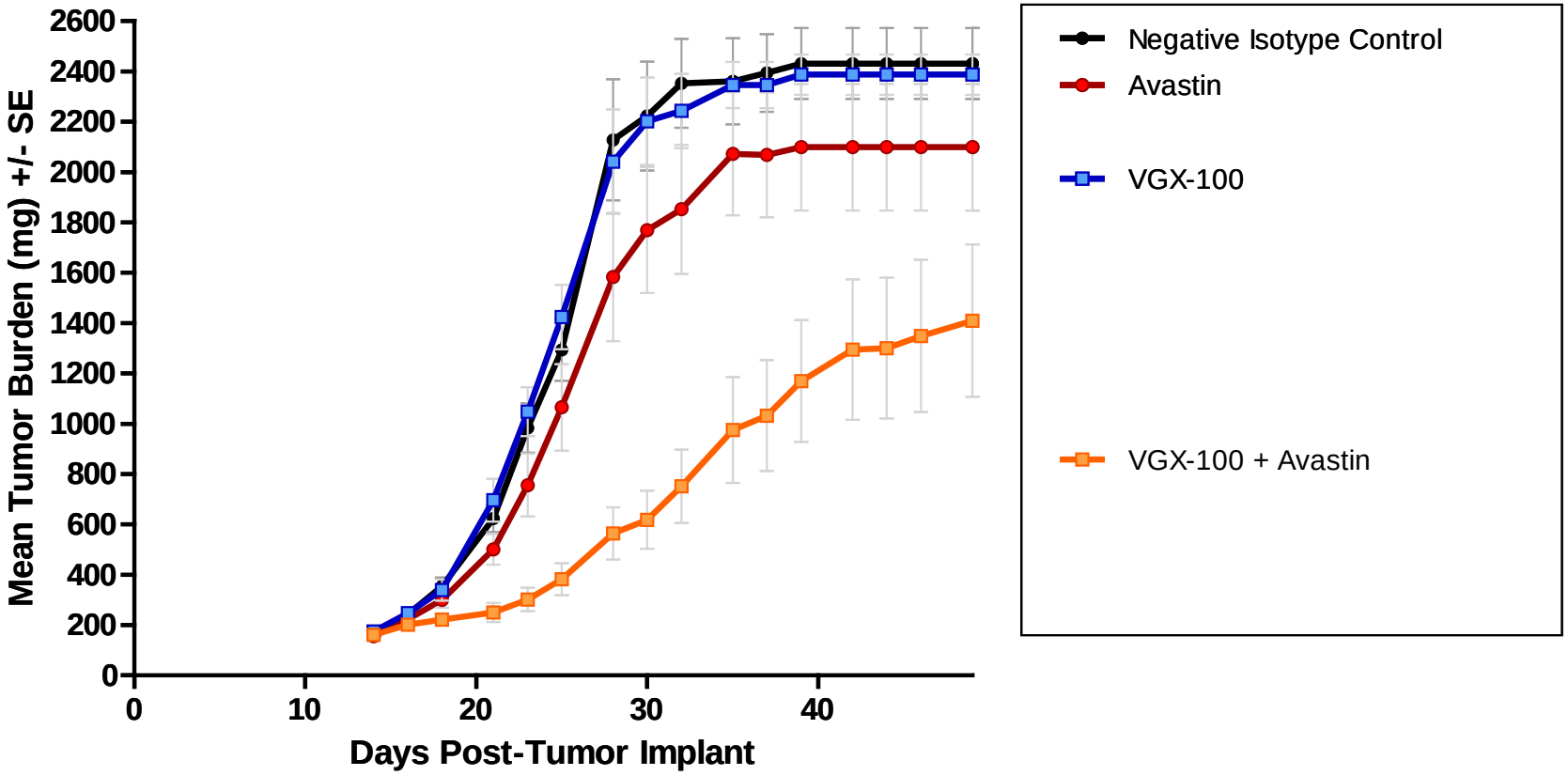


Plasma VEGF-C may be a predictive biomarker for the development of resistance to Bevacizumab

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).

VGX-100 Efficacy in Mouse Models of Human Cancer

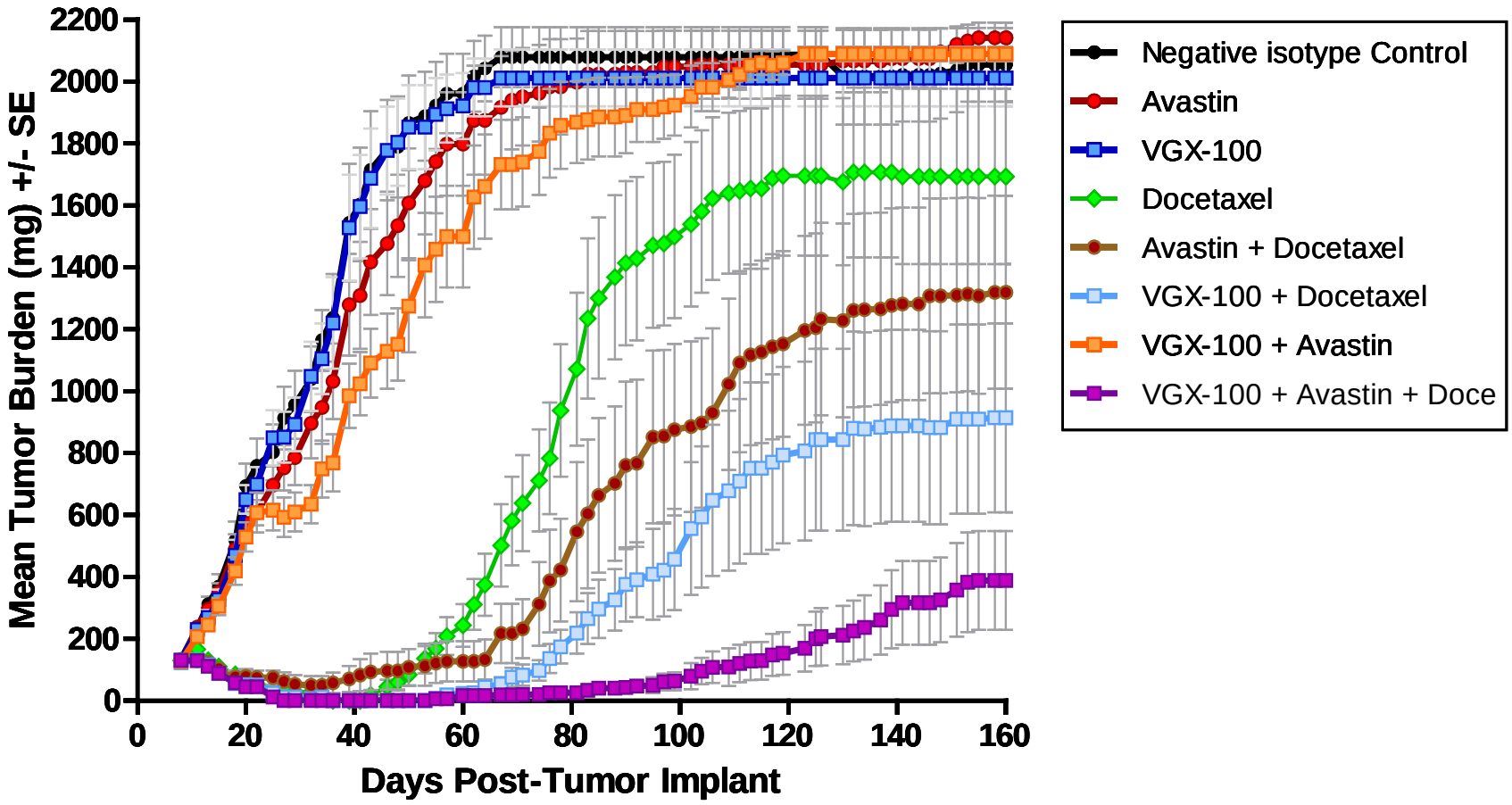
U87MG Glioblastoma Tumor Xenografts: VGX-100 effective in combination with Avastin



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

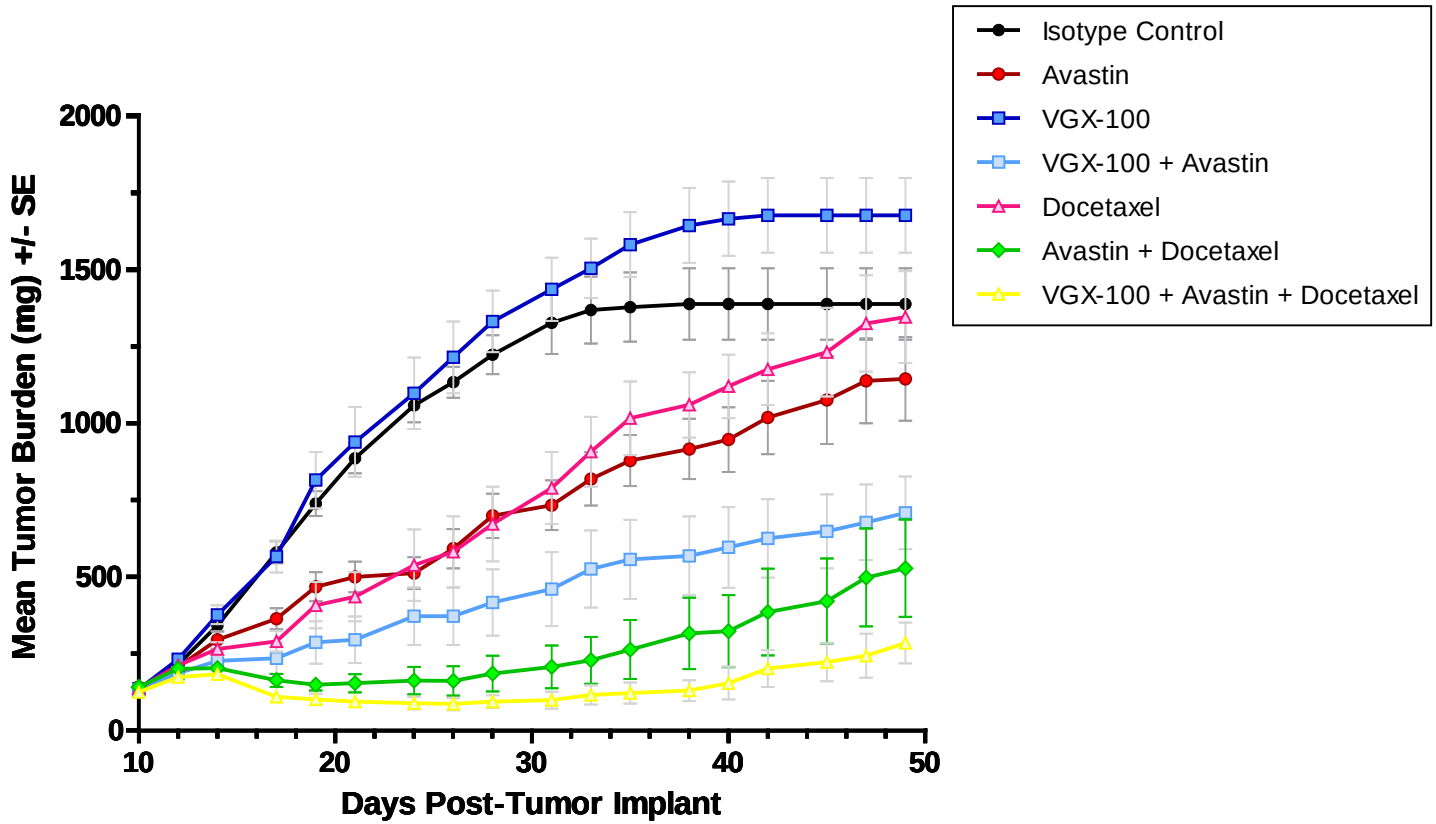
- 42% compared to control IgG
- 33% compared to single-agent Avastin.

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.

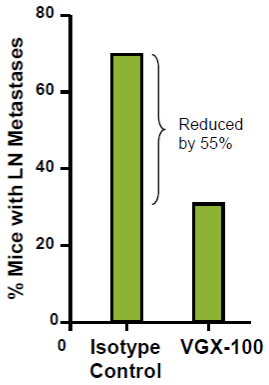
H292 NSCLC Tumor Xenografts: VGX-100 effective in combination with Avastin

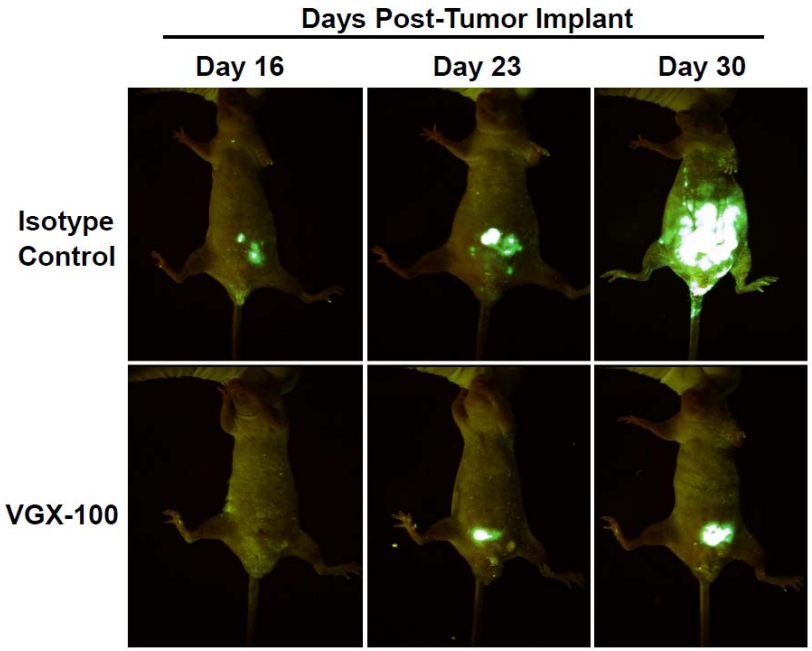


VGX-100 reduces metastasis in an orthotopic prostate cancer model

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 eg (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 SOC and anti-angiogenic agent
  - In the treatment of selected Avastin® resistant patients plus SOC

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
- Possibility for fast track registration based on increased PFS, OS in Phase 2b study when compared to Avastin alone
- 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.

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.

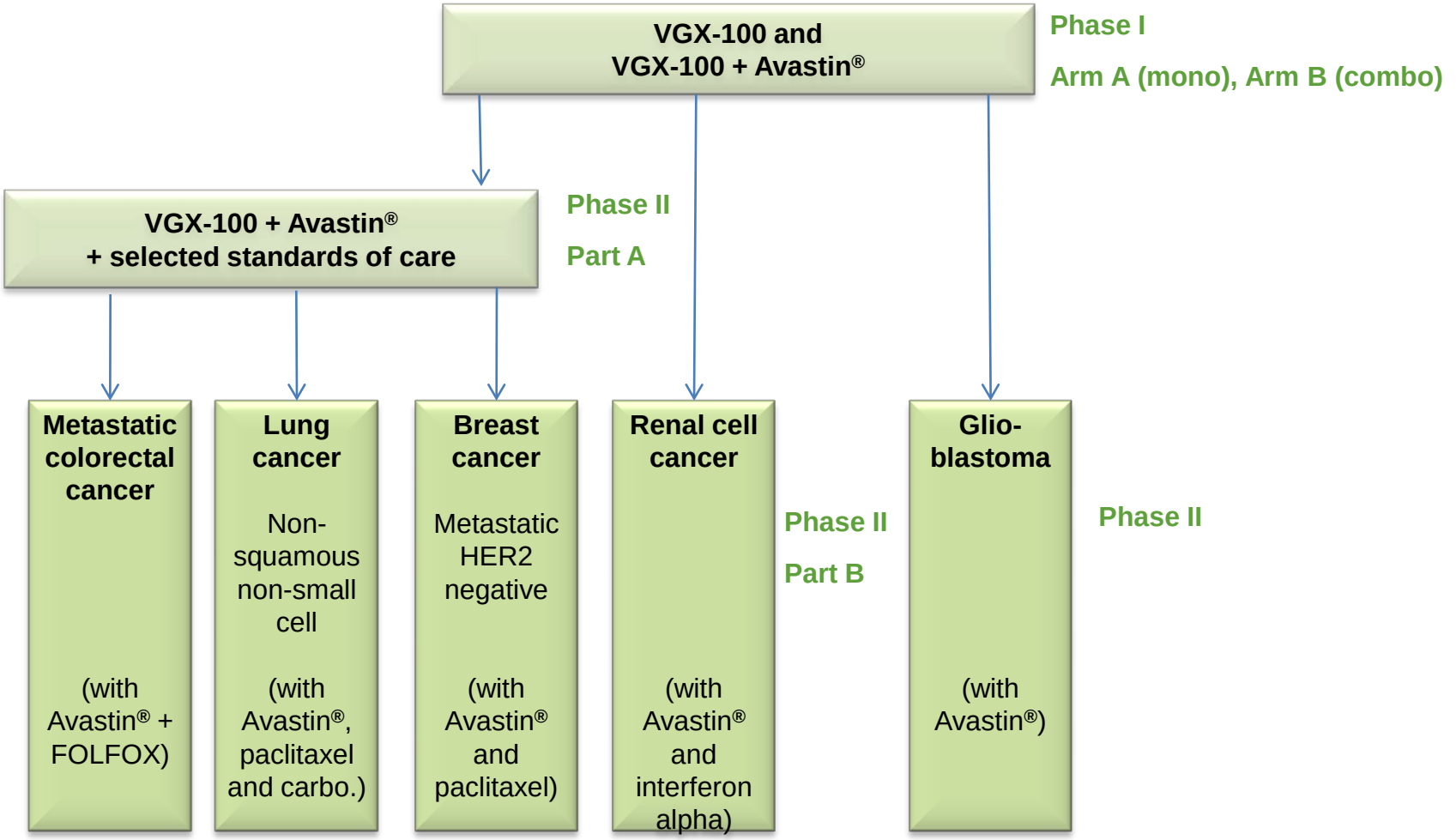
Patients and Methods

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.

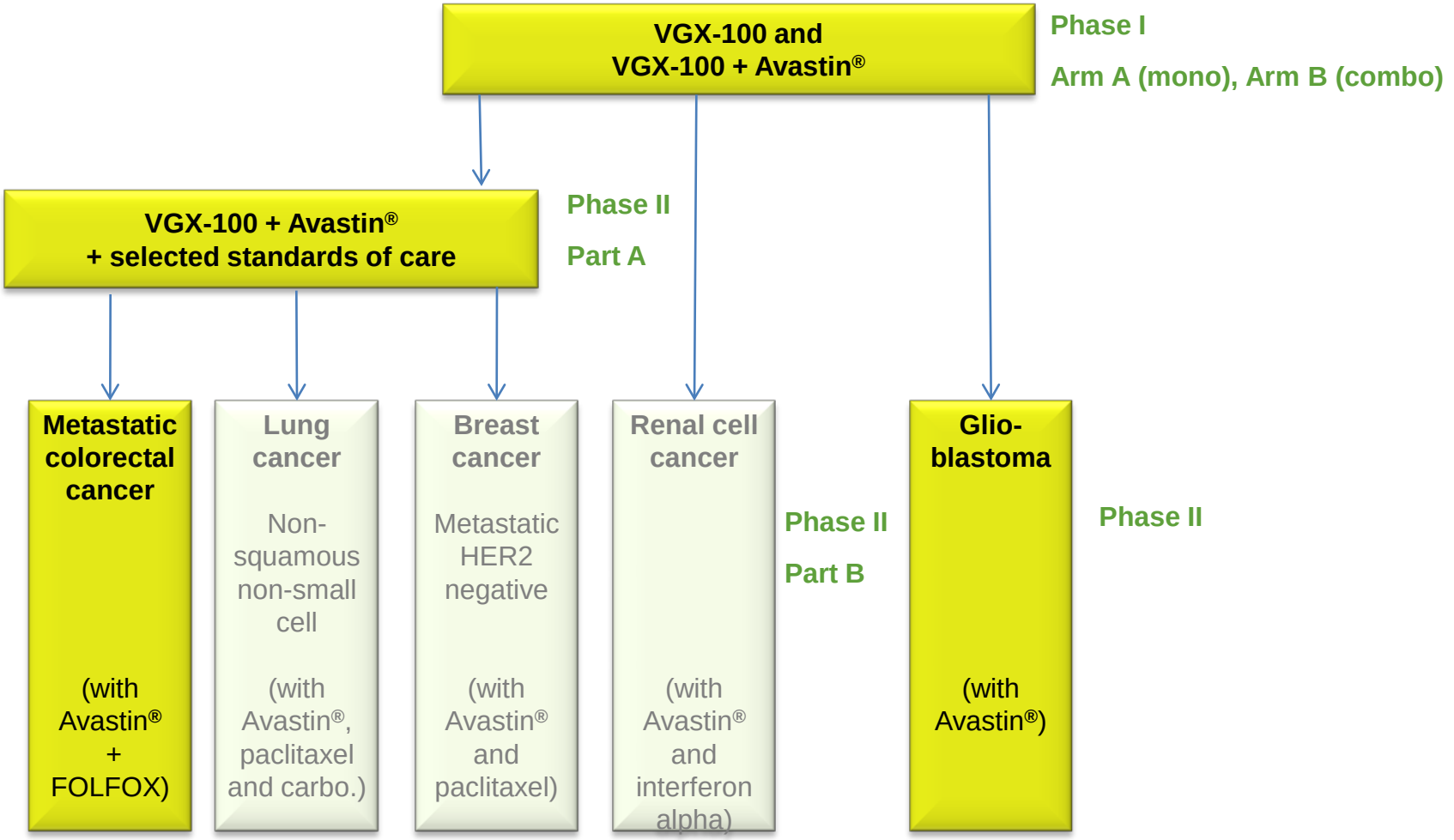
Results

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

Phase I and II clinical program



Phase I and II clinical program



VGX-100 OCULAR DEVELOPMENT OPPORTUNITY

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.

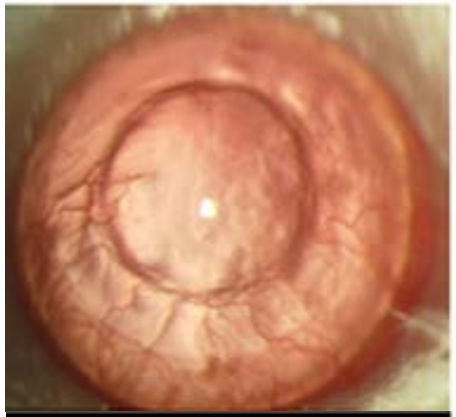
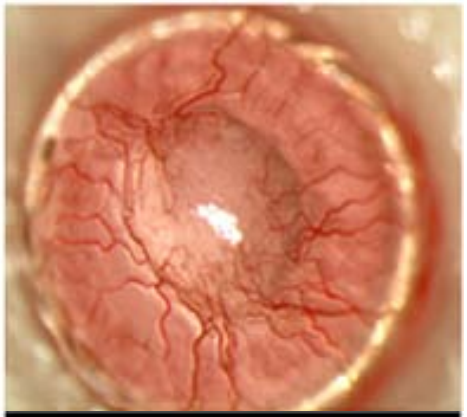
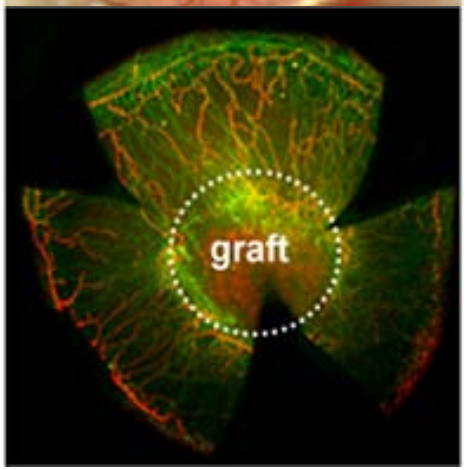
- Approx. 12 – 18 months to Phase I/II

Existing & Supportive Preclinical Data:

VGX-100 improves Corneal Transplant Survival

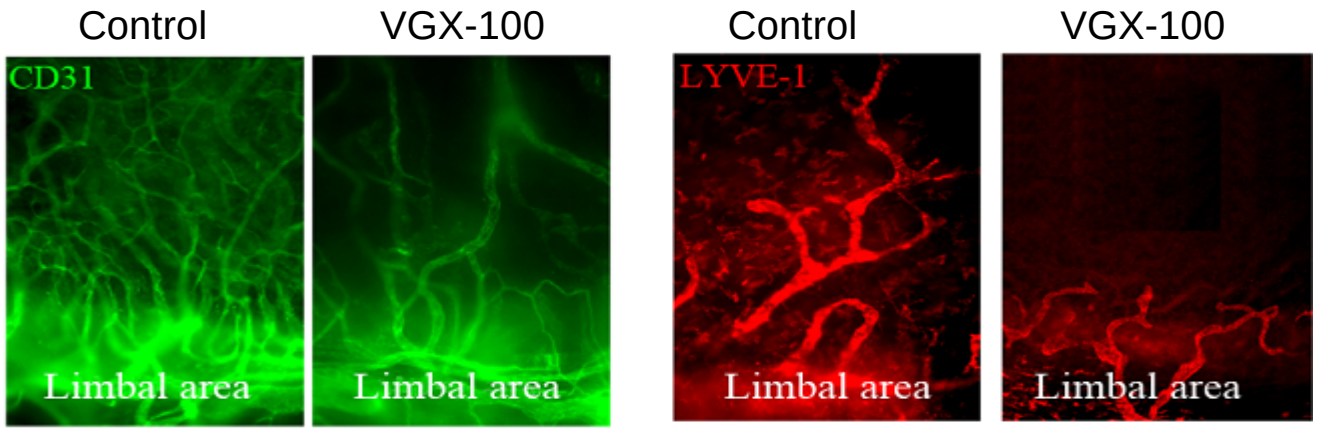
Rejected corneas are infiltrated by blood and lymphatic vessels and over-express VEGF-C and VEGFR-3

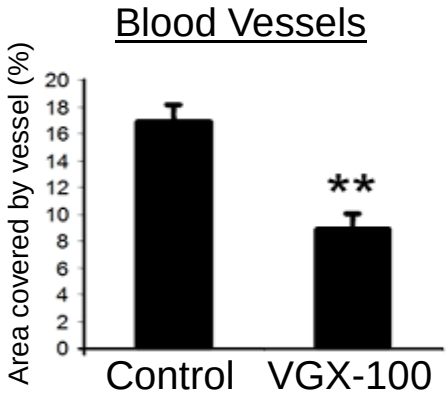
Transplanted Corneas: 3 wks Post-Transplant

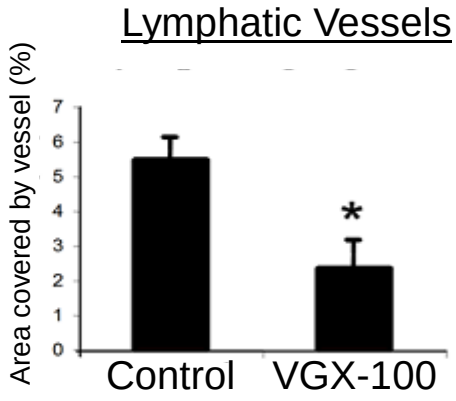
	ACCEPTED	REJECTED
Photomicrographs		
Flat-mount IHC stained corneas: **LYVE-1** (lymphatics) **CD31** (blood vessels)		

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

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

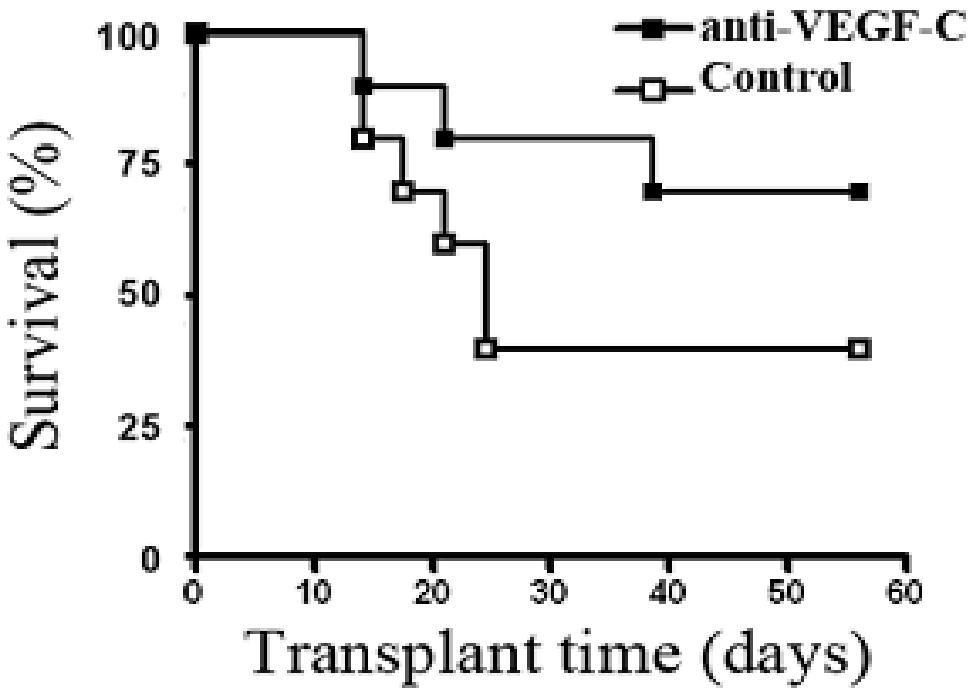






Day 7 post-transplant

VGX-100 Promotes Corneal Transplant Survival



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

Corporate Details

STATUS AND UPCOMING VALUE ADDING EVENTS

Activity	Timeline
VGX-100 First-in-human cancer patients Clinical Study (monotherapy)	Q4 2011
CUP Test Launch	Q1 2012
VGX-100 First-in-human cancer patients Clinical Study (Combination with Avastin/Chemotherapy)	H2 2012
VGX-100 Phase 1 trials complete	Q4 2012
IMC-3C5 Phase 1 trials reported	H1 2013
VGX-100 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

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 @ 7 October 2011 (unaudited)

Stock code:	**CIR**
Share price:	50c (AUD)
Shares issued + deferred issue:	46,396,928
Market cap:	~ A$23 mill
Cash holdings: Listed investments: (ASX: ANP, OIL)	~ A$20 mill A$2.0M

Cash Burn estimate 2011/12 $10-12m

Institutions/Funds: ~ 43%

Retail investors: ~ 30%

Professional investors: ~ 27%

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 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 (Avastin responders)
  - 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 in Q4 2011
  - OIL culmination of “strategic review” in Q4 2011

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

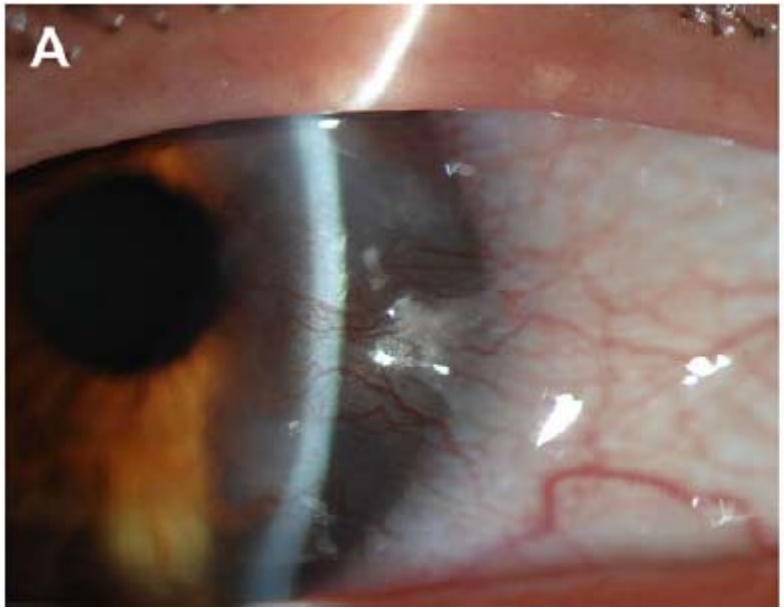
- **Capability to get to key value adding events**
  - Approx $22M in cash and investments
  - Superb internal and external drug development teams

Thank You

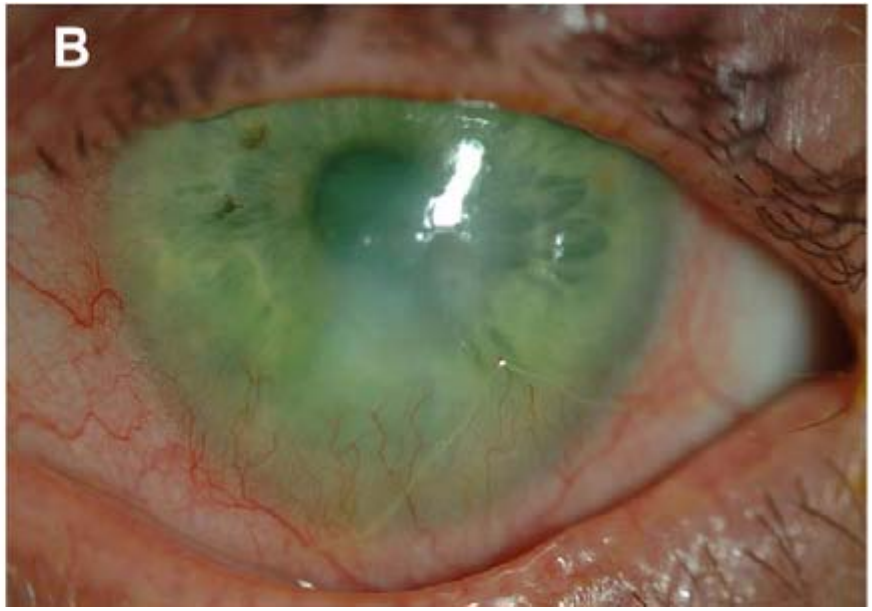
www.circadian.com.au

Appendix

Clinical Appearance of CNV in Inflammatory Disorders



CNV in Salzmann's nodular degeneration

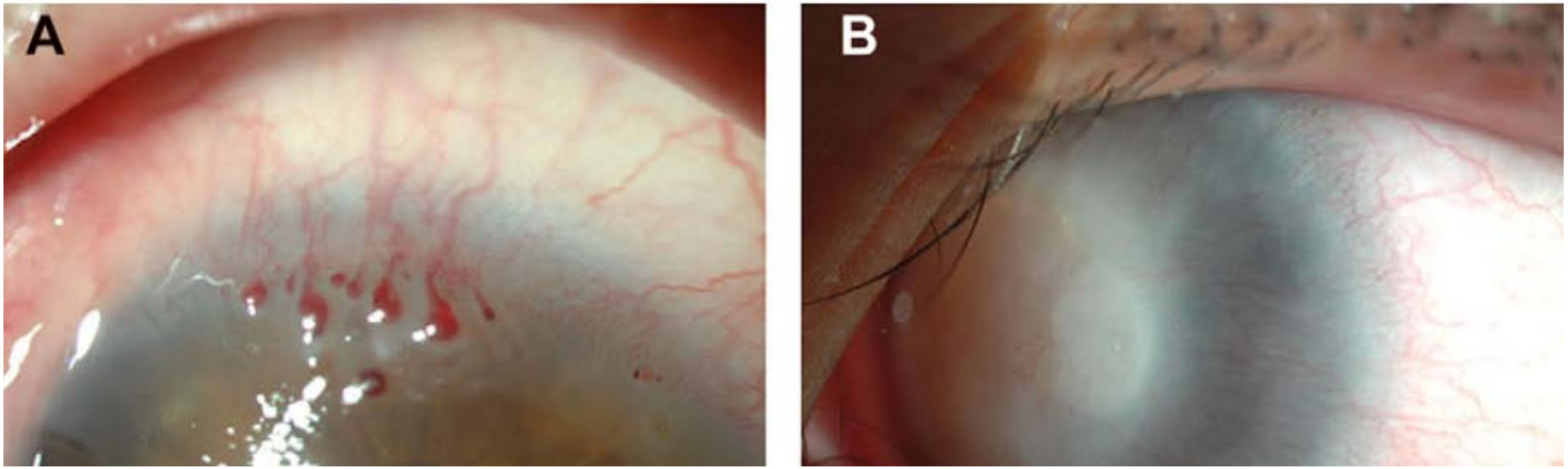


CNV due to Rosacea

Ellenberg et al., Prog.Retinal & Eye Research, 29:208-248, 2010.

CNV and Inflammation Associated with LSCD

Ellenberg et al., Prog.Retinal & Eye Research, 29:208-248, 2010.



CNV due to Limbal Stem Cell Deficiency

CNV can be diagnosed & monitored using routine procedures:

- Ocular examination
- Corneal fluorescein staining & slit-lamp
- Quantitation of vascularised corneal area, depth and stromal involvement

Preliminary Market Opportunity Assessment

CNV associated with Ocular Herpes Simplex Infection:

Incidence of New & Recurring Herpetic Keratitis Cases/Year (U.S.A.): 50,000	
Annual Cost per Patient/Year (U.S.A.)	Estimated Annual Revenue (U.S.A.)
• USD 5,000	USD 250M
• USD 10,000	USD 500M
• USD 15,000	USD 750M

Preliminary Market Opportunity Assessment

Corneal Allograft Rejection:

# Corneal Transplants/Year (U.S.A):	40000
# High-Risk Corneal Transplants/Year (U.S.A):	10000
Annual Cost per Patient/Year (U.S.A)	Estimated Annual Revenue (U.S.A.)*
• USD 5000	USD 50M
• USD 10000	USD 100M
• USD 15000	USD 150M

Comparables

- Market Cap Comparable
  - Bioinvent, (Nasdaq OMX Stockholm: BINV SS), has been trading with a market cap in the range of $275 million
  - 4 products in either FDA Phase I or II trials including TB-403
  - TB-403, at Phase I, is a humanized monoclonal antibody developed to treat solid tumours in combination with Avastin and chemotherapy
- Licensing Comparable
  - Astellas Pharma's $1.3 billion milestone licensing agreement with Aveo Pharmaceutical for a FDA Stage III VEGF antibody for renal cancer
  - Bioinvent/Roche Deal on PLGF Ab
- Acquisition Comparable
  - Arius Research, a Canadian development stage antibody company, bought by Roche in July 2008 for $189 million
  - Portfolio of pre-clinical stage antibody candidates

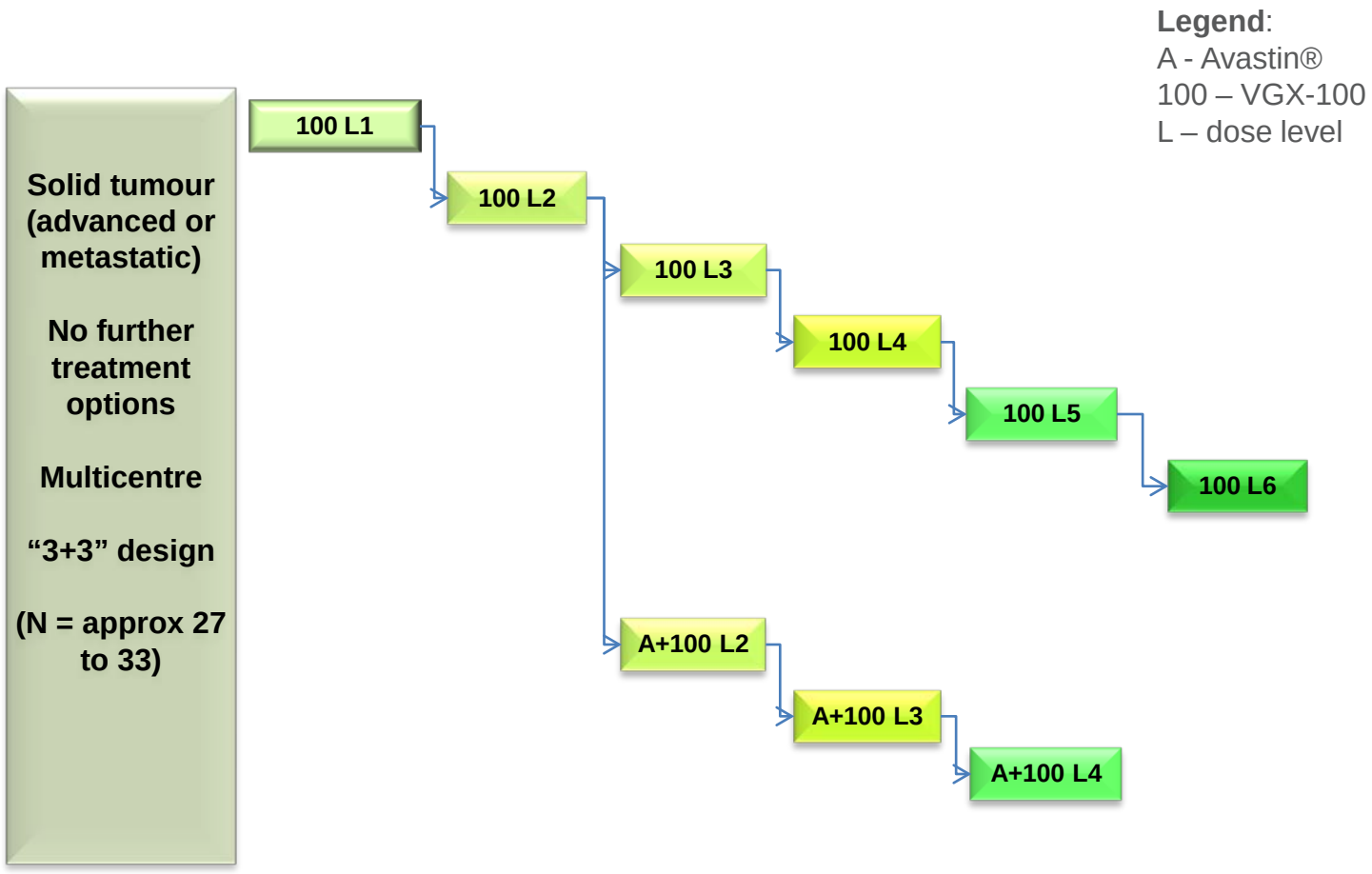
Competitive Landscape
BIOLOGICAL ANTI-ANGIOGENIC AGENTS

Company	Molecule	Target	Partner & Partnering Stage	Clinical Stage	Indication	Relevance To CIR
Regeneron	Aflibercept (VEGF Trap)	VEGF-A PlGF	Sanofi Phase 1	P3	1st and 2nd line CRC 2nd line NSCLC 1st line hormone resistant prostate cancer	Positioned as direct competitor to Avastin, NOT as complementary agent
Regeneron	Aflibercept	VEGF-A PlGF	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	PlGF	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

Dominant and protected IP position

- Granted IP rights in major territories to VEGF-C/D proteins and VEGFR-3 and blockers
- Freedom to operate through deals with HGS and Chugai
- IP rights over product candidates extend beyond September 2023
- Further strategic IP filings being made to extend patent life
- Over 500 granted and pending patents worldwide
- Protection through US and European market exclusivity provisions

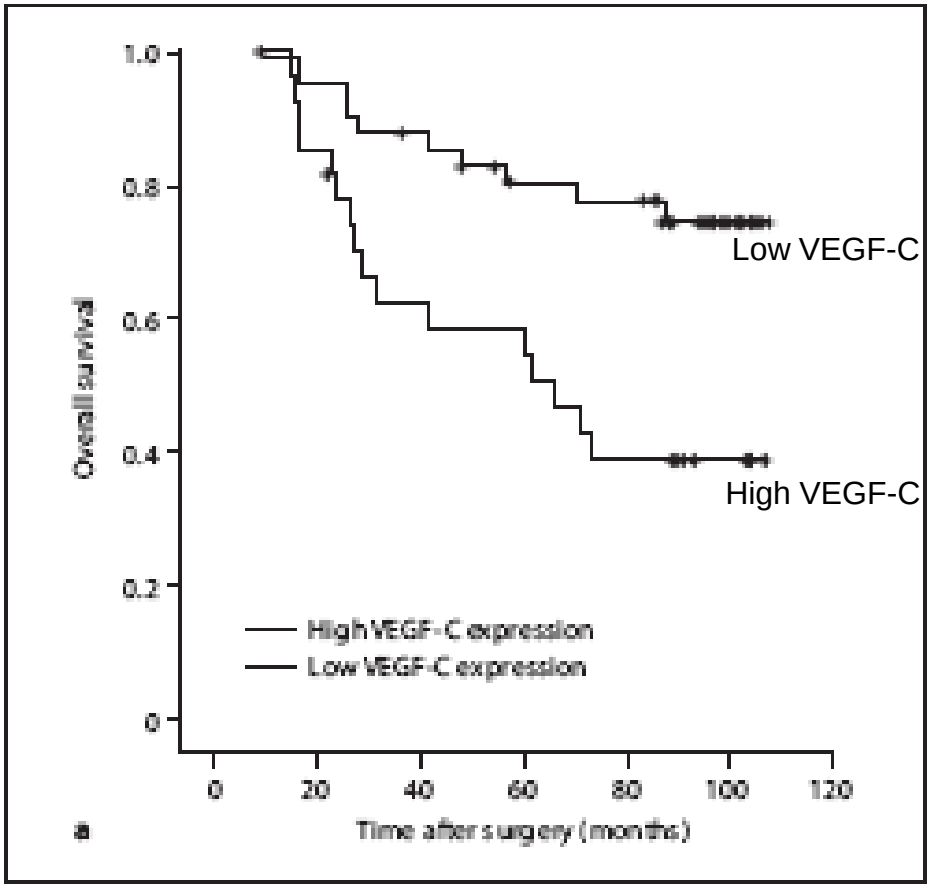
Phase I First-in-Human Study



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

One example

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.