ASX and Media release

16 June 2011

Circadian provides market update on clinical development plans for VGX-100 in oncology and eye disease indications

Circadian Technologies Limited (ASX.CIR, OTCQX.CKDXY) provided a market update presentation to shareholders and market participants today on the clinical developments plans for its lead VEGF-C antibody therapeutic candidate –VGX-100 – over the next 2-4 years.

A copy of the presentation is attached.

It can also be accessed via the company's website www.circadian.com.au

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About Circadian Technologies Limited

Circadian (ASX:CIR) is a biologics drug developer focusing on cancer therapies. It controls exclusive worldwide rights to a significant intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF) C and D. The applications for the VEGF technology, which functions in regulating blood and lymphatic vessel growth, are substantial and broad. Circadian's internal product development programs are focussed on novel anti-cancer therapeutics for large unmet needs. Circadian has also licensed rights to some parts of its intellectual property portfolio for the development of other products to ImClone Systems, a wholly-owned subsidiary of Eli Lilly and Company, including the antibody-based drug IMC-3C5 targeting VEGFR-3.

About Circadian's pipeline of treatments for cancer

The clinical and outstanding commercial success of Avastin®, an antibody that blocks the activity of VEGF-A, clinically validated anti-angiogenic drugs as an effective means of inhibiting solid tumour growth. By blocking the interaction of VEGF-A with its receptors, primarily VEGFR-2, the multi-billion dollar cancer therapeutic slows tumour growth by inhibiting blood vessel recruitment into the tumour, effectively starving tumours of essential nutrients and oxygen required for growth. Avastin®, which is sold by Genentech, now part of Roche, had U.S. sales in 2009 of US$5.7 billion and worldwide sales in excess of US$8.6 billion. Avastin® is approved by the US FDA in the following indications: metastatic colorectal cancer, non-squamous-cell lung cancer, metastatic breast cancer, glioblastoma, metastatic renal cell carcinoma.

The VEGF-C inhibitor, VGX-100, a key therapeutic in Circadian's portfolio, block this alternative stimulator for VEGFR-2. As such, it has the potential to block blood vessel growth in tumours resistant to anti-VEGF-A therapy and, when used in combination with drugs like Avastin®, may completely shut down angiogenesis (the growth of blood vessels) mediated by VEGFR-2, resulting in greater clinical efficacy.

VEGF-C along with the molecule VEGF-D. are also the only known proteins to bind and activate VEGFR-3 which drives lymphatic vessel and tumour-associated blood vessel growth. Inhibitors of VEGF-C thus have therapeutic potential to inhibit not only primary tumour growth through their anti-angiogenic activities, but to also inhibit tumour spread or metastasis via the lymphatic vessels - a mechanism of tumour dissemination that is often the deadliest aspect of many tumour types and a mechanism that is not effectively blocked by anti-VEGF-A or anti-VEGFR-2 therapeutics.

Inherent risks of Investment in Biotechnology Companies

There are a number of inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Circadian are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in companies specialising in drug development must be regarded as highly speculative. Circadian strongly recommends that professional investment advice be sought prior to such investments.

Forward-looking statement

Certain statements in this ASX announcement may contain forward-looking statements regarding Company business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent

in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Circadian undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Actual results could differ materially from those discussed in this ASX announcement.

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ABN 32 006 340 567

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

Market Update

June 16, 2011

Robert Klupacs, CEO

Mark Sullivan, Head of Development

Megan Baldwin, Head of Preclinical R&D

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.

The Journey

3 years ago we undertook a radical change in strategy:

To take an extensive and tremendously exciting early stage IP portfolio in the field of angiogenesis and lymphangiogenesis, which had been transformed by the emergence of drugs such as Avastin® and Sutent®

AND

To convert it into therapeutic and diagnostic products which could improve the treatment of cancer and potentially other serious diseases.

The issues we needed to address

- What is our niche?
- What will be our product?
- How best to develop?
- Who best to develop for?
- Cost of development?
- Time of development?
- Getting the expertise to develop

Our Product (s)

- A VEGF-C antibody used in conjunction with standard of care chemotherapy, which includes anti-angiogenic agents (“VGX-100”)
- VEGF-C and VEGF-D diagnostics which can help identify patients likely to most benefit from our therapy
- Other cancer diagnostics to give us presence in the clinical oncology setting and also provide ongoing revenues

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.

Today

1. The rationale for the role of VEGF-C inhibition as a cancer therapeutic and supporting pre-clinical data – Dr Megan Baldwin

2. VGX-100 development to date and clinical development plans in oncology – Mr Mark Sullivan

3. The opportunity and development pathway for VGX-100 in “front of the eye” disease – Dr Megan Baldwin

4. Wrap Up and Q&A

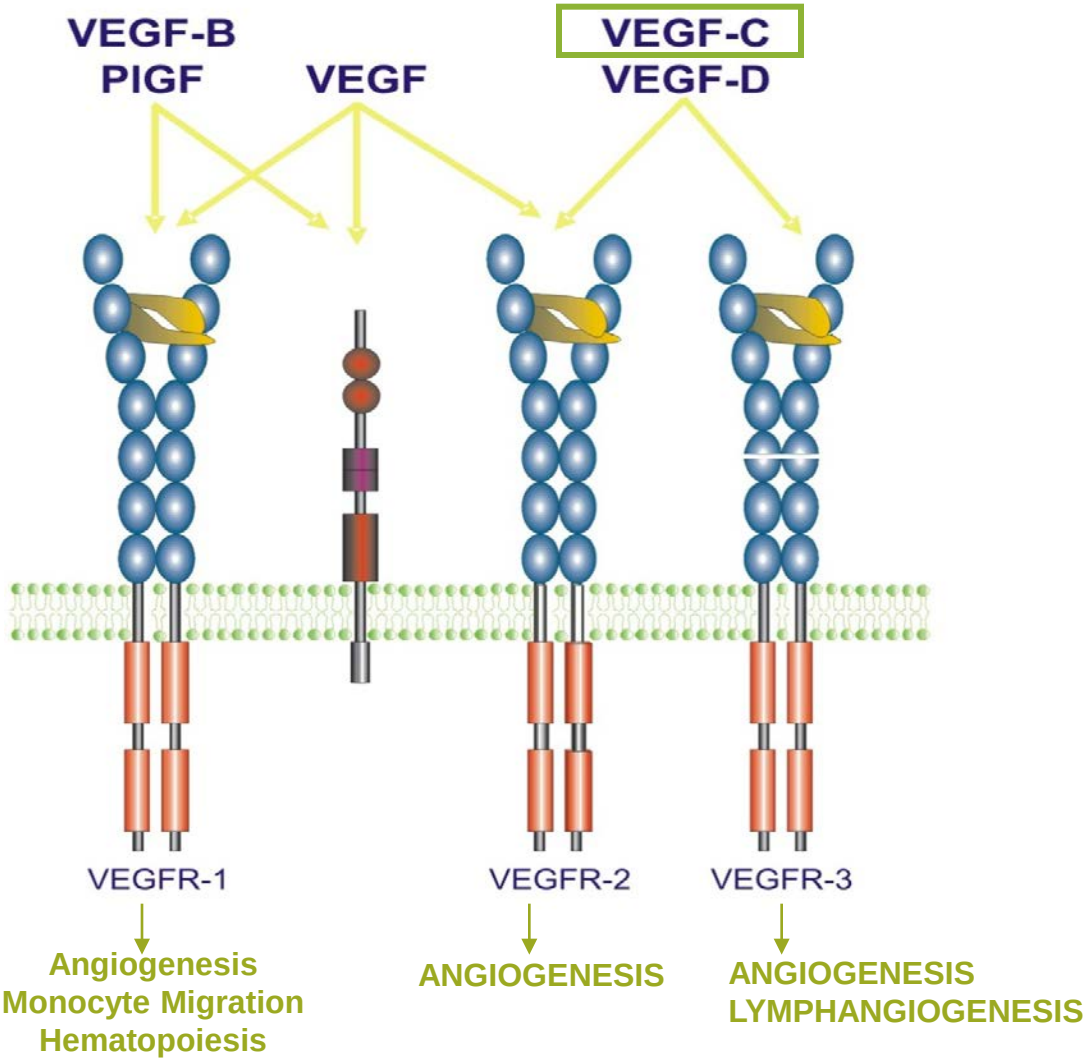
VEGF-C Inhibition: Rationale

Dr Megan Baldwin
Head of Preclinical R&D

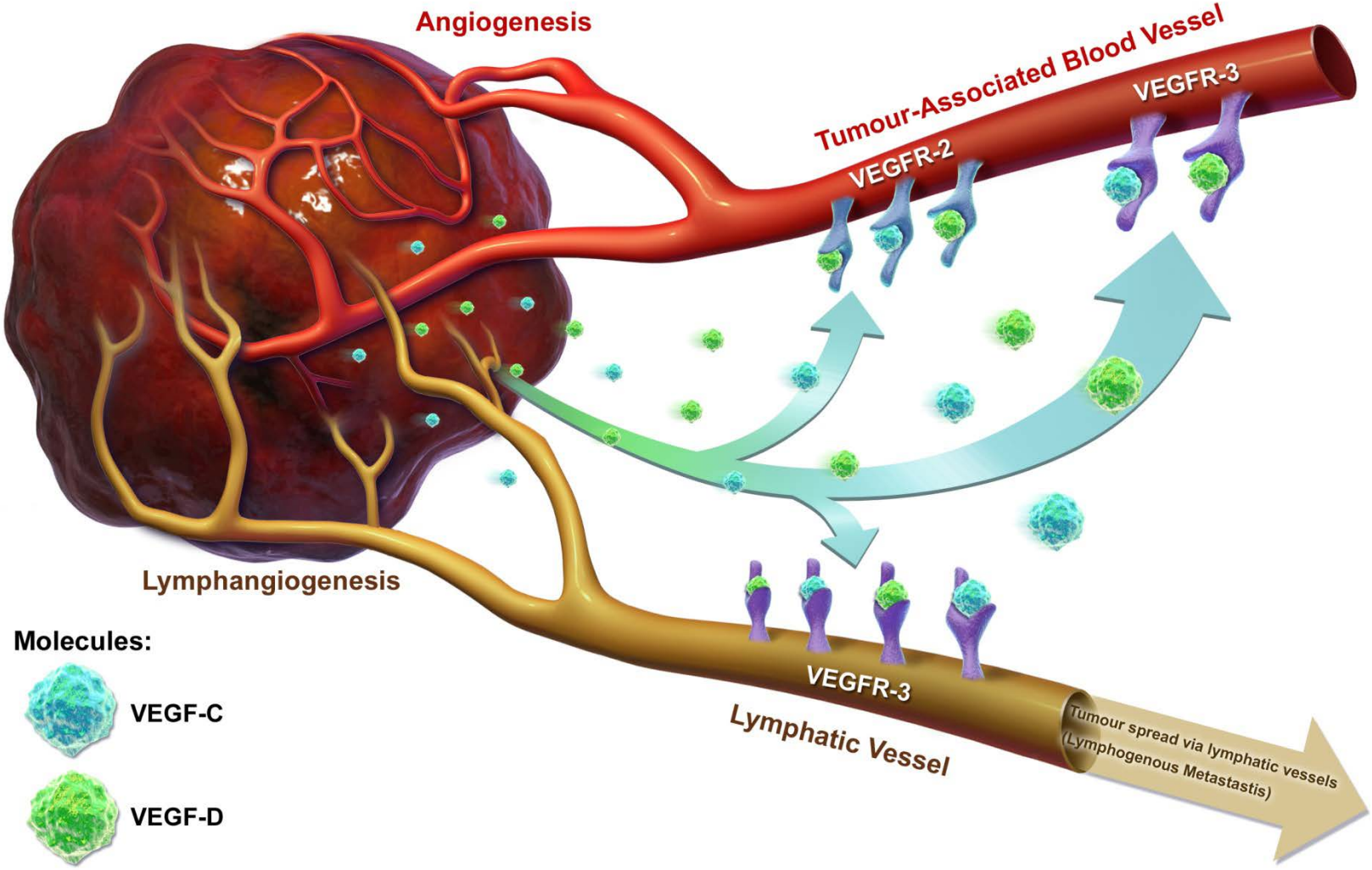
VGX-100 Program

- VGX-100 is a fully human, high affinity, neutralising monoclonal antibody for VEGF-C.
- Development and clinical program designed to improve anti-angiogenic therapies for cancer and eye disease.
- Preclinical data demonstrating inhibition of primary tumor growth in several mouse xenograft models.

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



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



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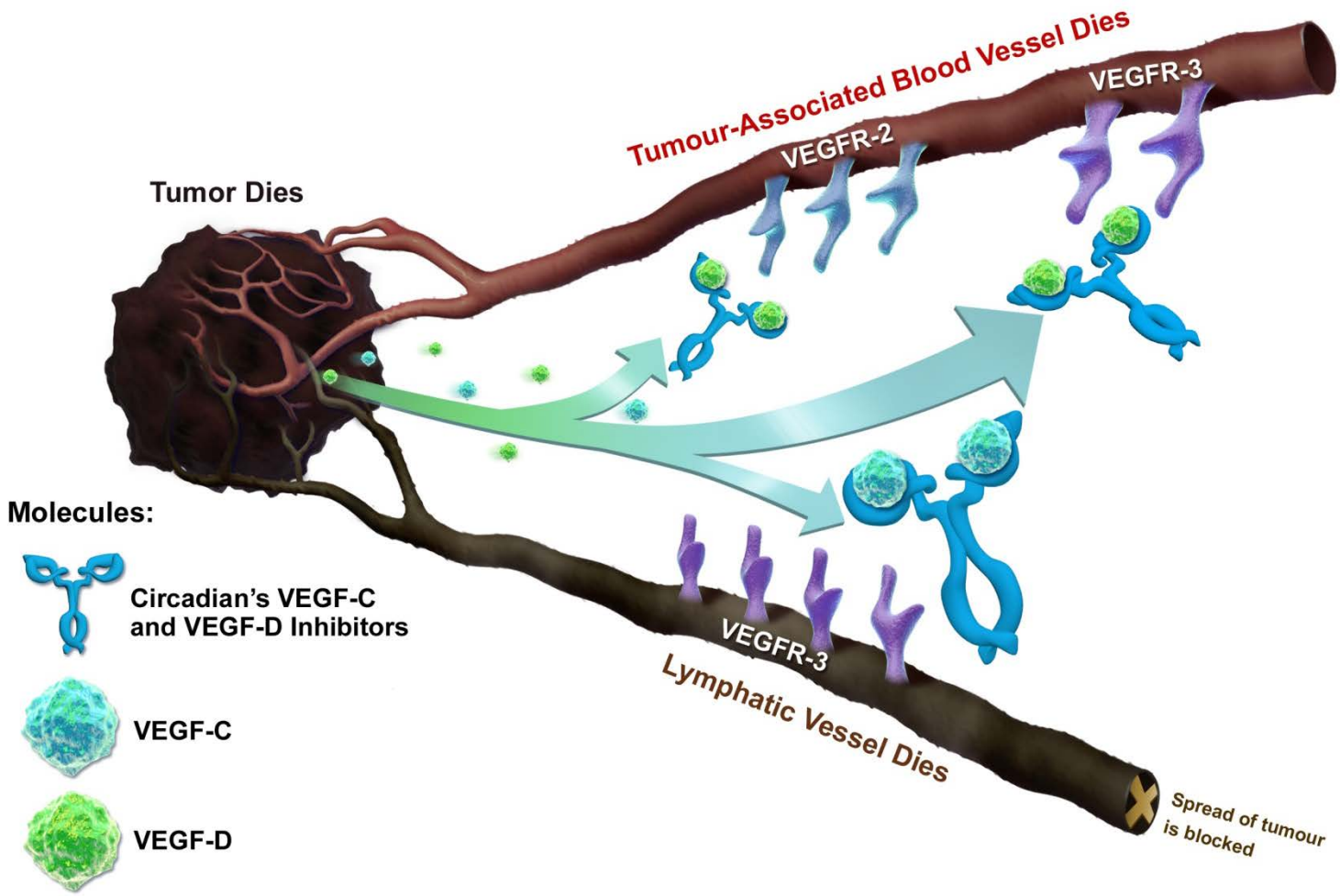
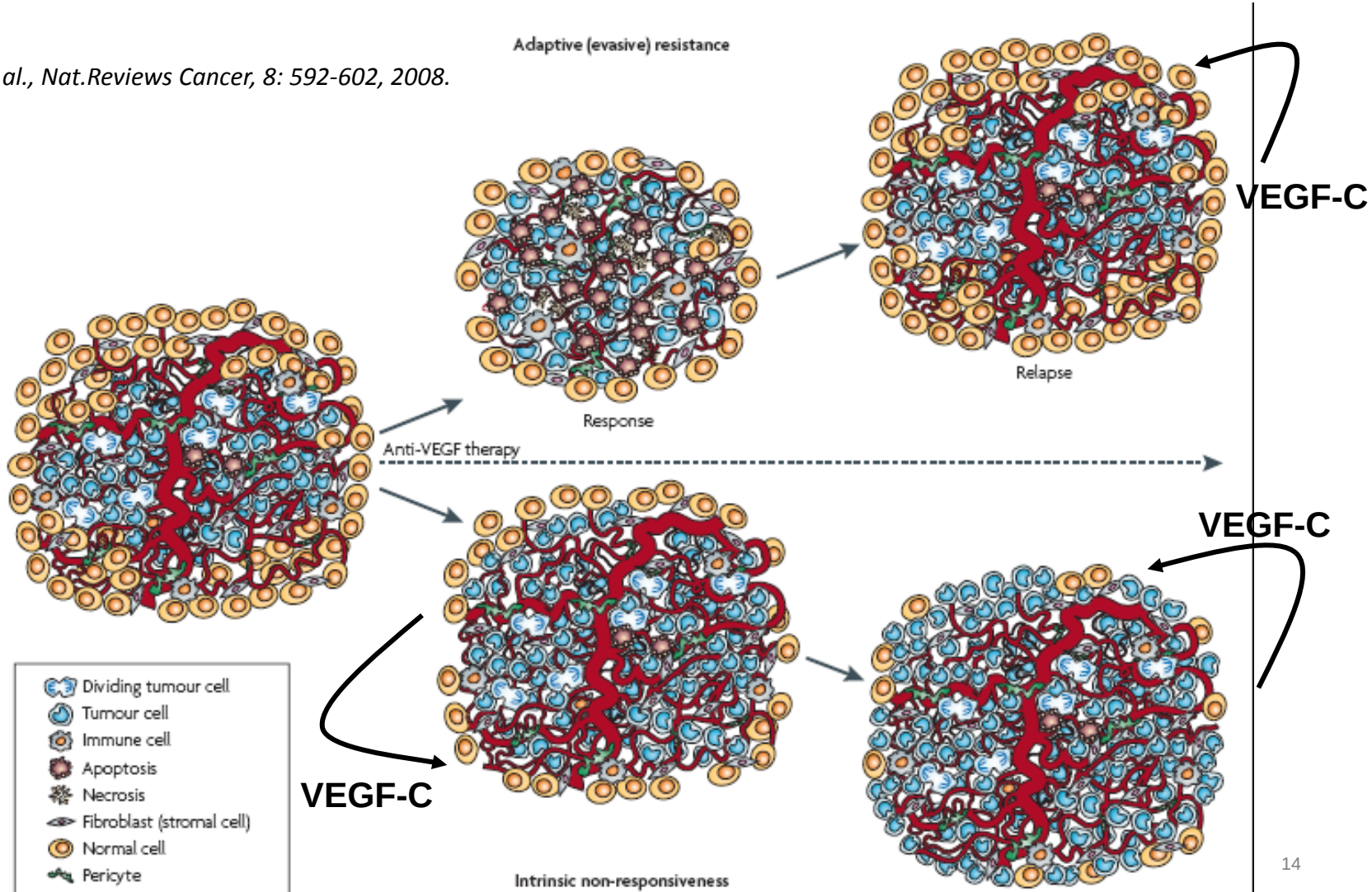


VEGF-C in Avastin® ‘escape’

- 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 signaling through VEGFR-2, despite VEGF inhibition.

Our Approach:
Targeting Resistance to Anti-VEGF Therapy

Bergers et al., Nat.Reviews Cancer, 8: 592-602, 2008.

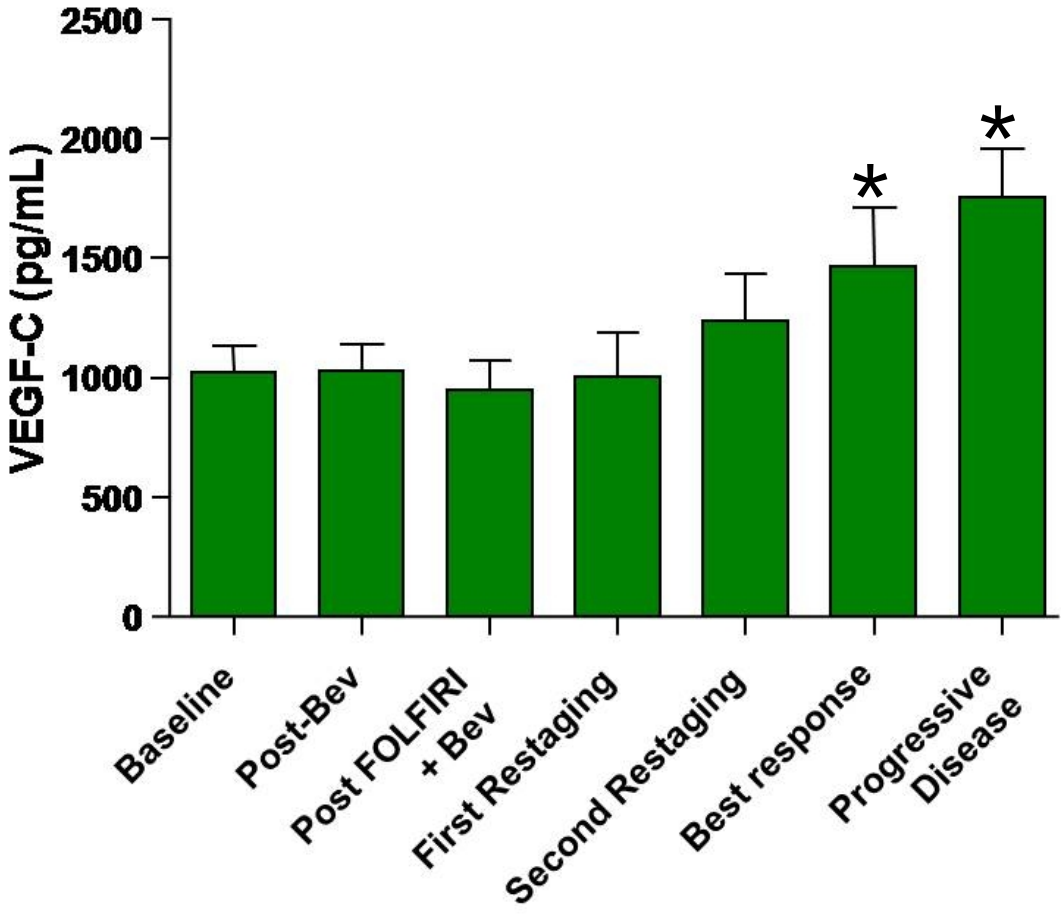


VEGF-C in Avastin® 'escape'

- Collaborative study with the MD Anderson Cancer Center
- Multiple samples were taken from each patient prior to and during the course of their treatment and disease course*.
- 42 patient cohort
- Circulating levels of VEGF-C significantly elevated in patients treated with Avastin®/FOLFIRI just prior to the onset of progressive disease.
- **This data implicates VEGF-C as a key mediator driving tumor growth in Avastin® relapsed/refractory patients.**

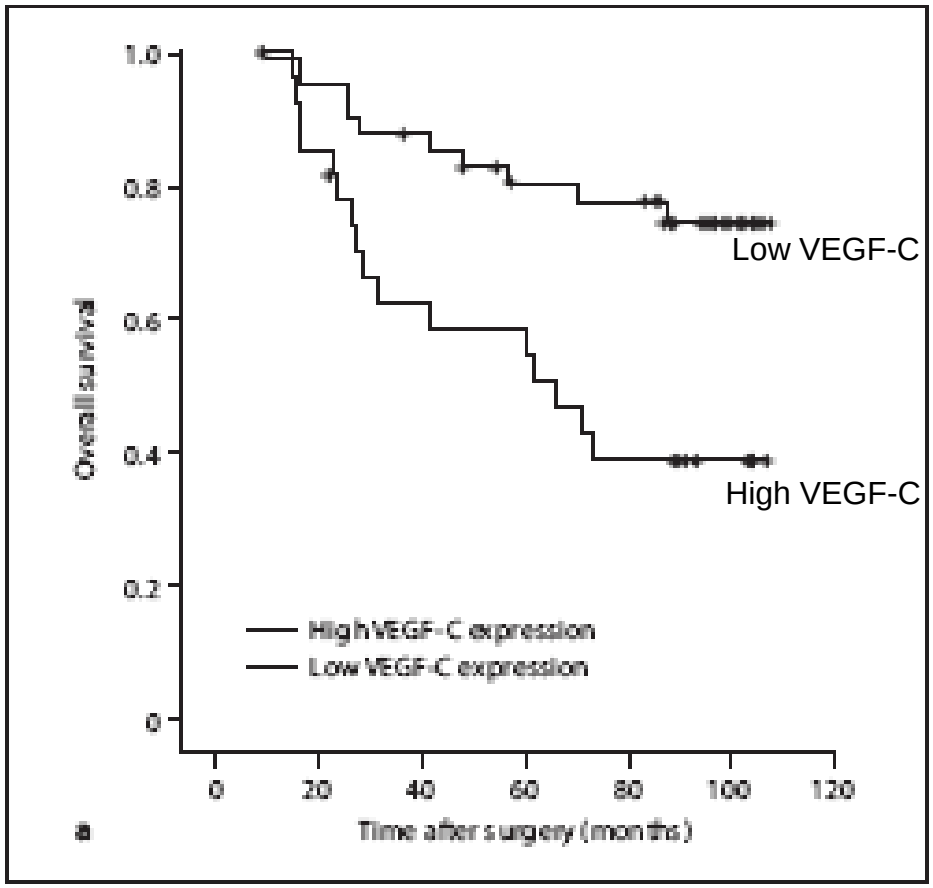
* Kopetz et al., JCO, 28(3): 453-9; 2010.

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



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 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

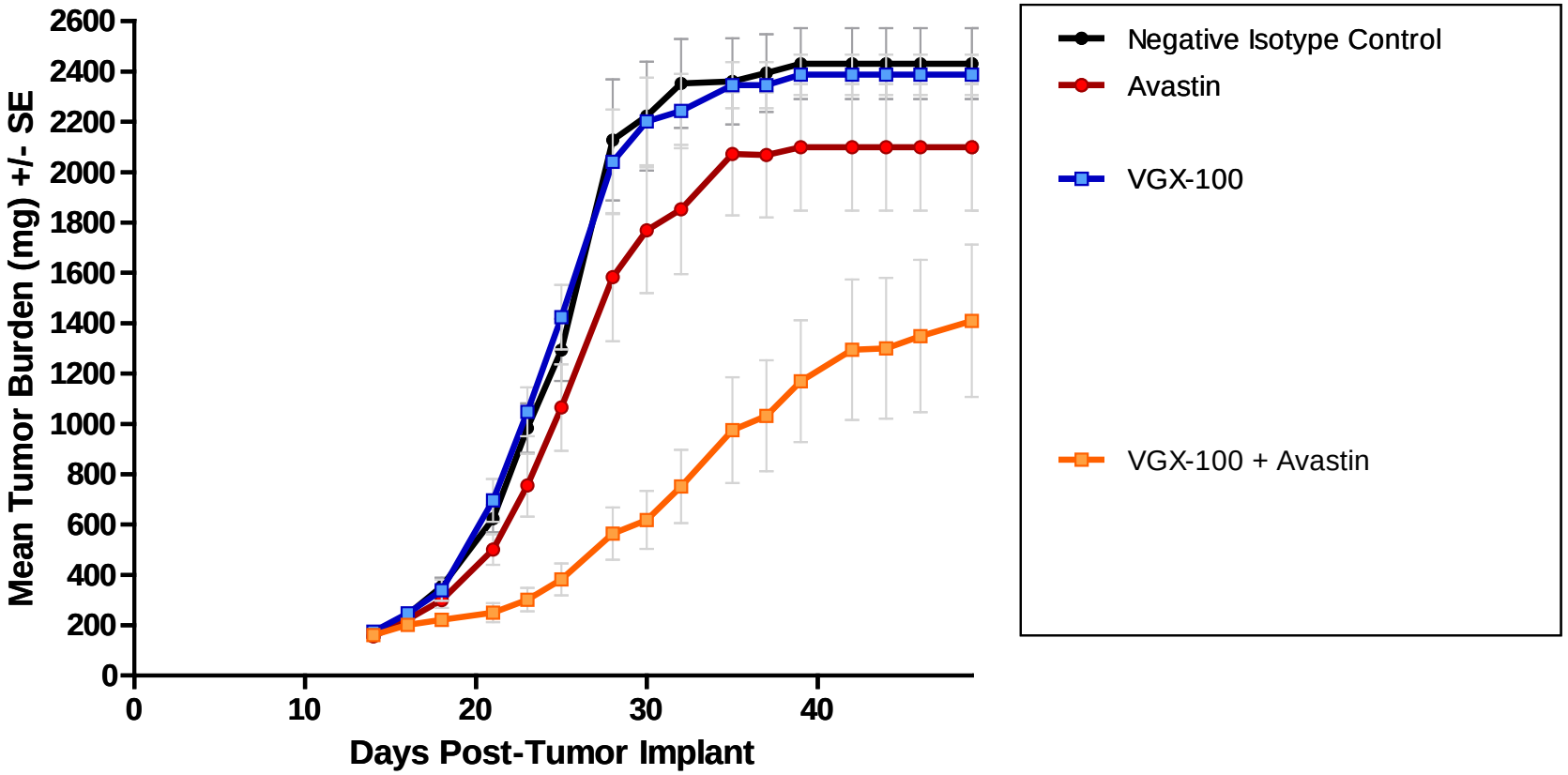
Hu et al., Eur Surg Res, 39: 229-238, 2007.

VGX-100 Efficacy in Mouse Models of Human Cancer

VGX-100 Inhibits Tumor Growth in Mouse Models of Human Cancer

- VGX-100 has inhibitory activity in a wide variety of human tumor xenografts, including:
  - Prostate
  - Glioblastoma
  - Lung
  - Ovarian
  - Pancreatic
  - Breast

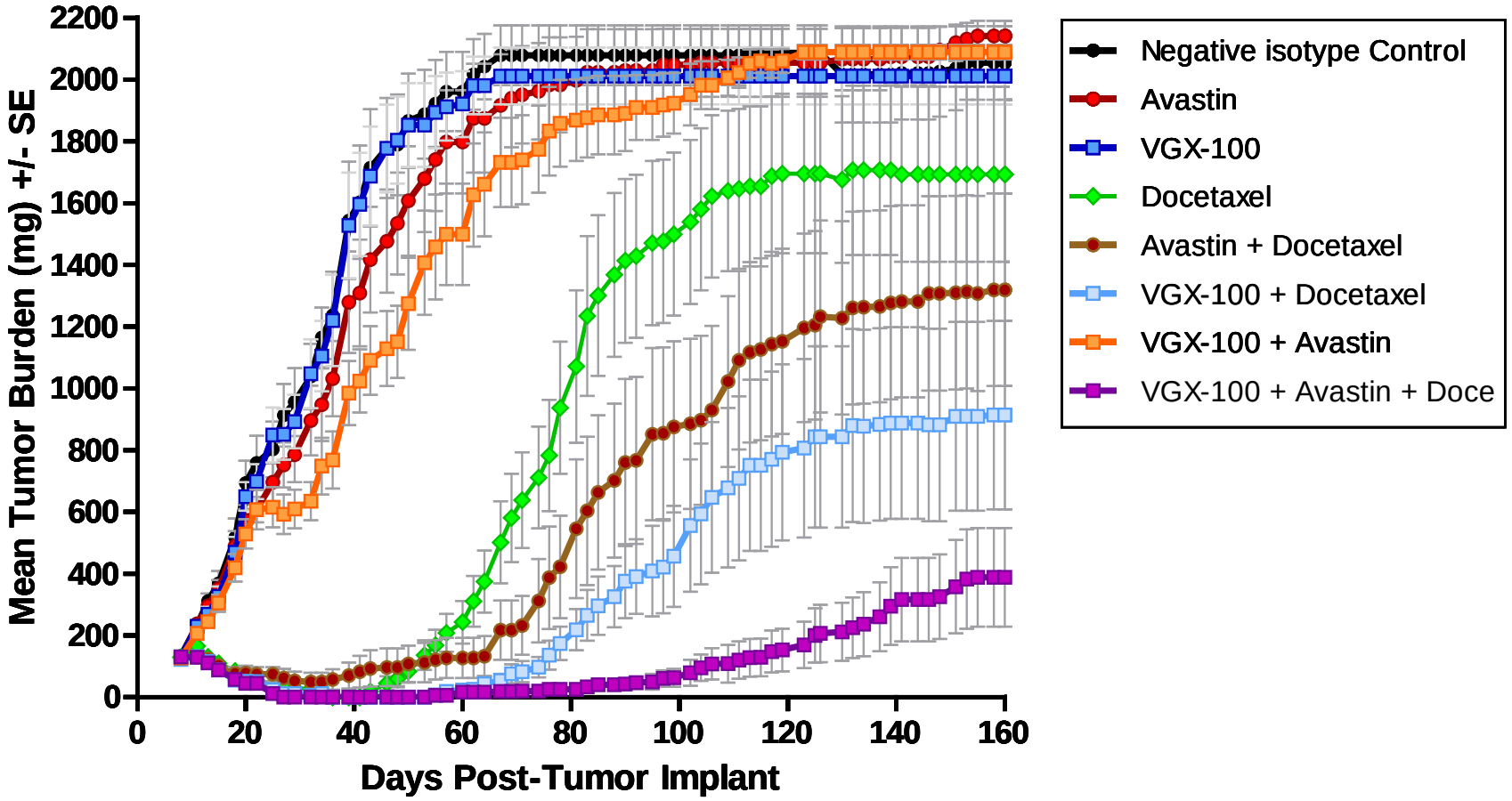
U87MG Glioblastoma Tumor Xenografts: VGX-100 effective in combination with Avastin



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

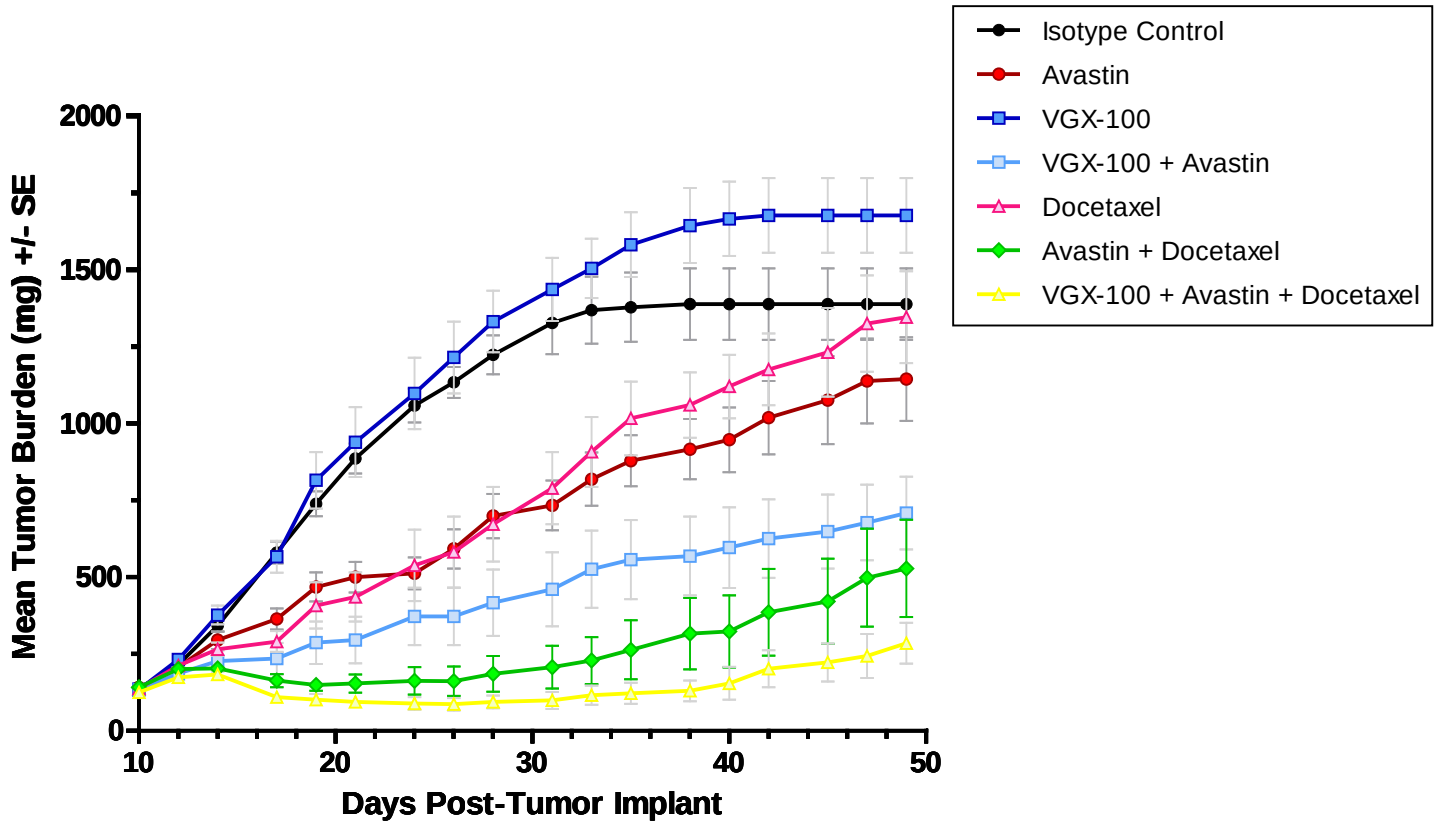
- 42% compared to control IgG
- 33% compared to single-agent Avastin.

VGX-100 single-agent & combination therapy in PC-3 prostate cancer xenografts

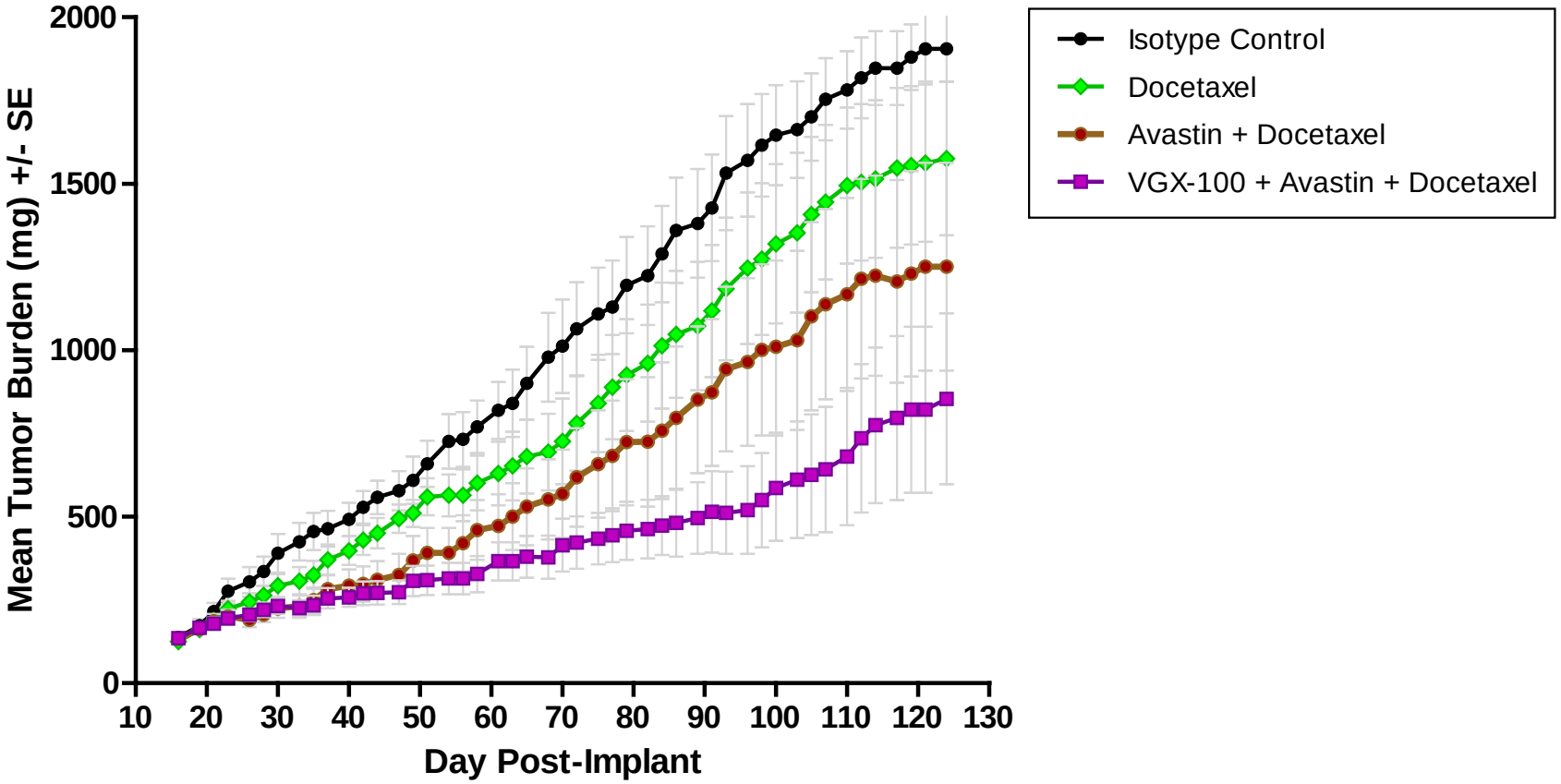


Docetaxel: Weekly IV at 10 mg/kg for 3 weeks. Vehicle: 10% EtOH, 10% Tween 20, 80% water.

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



VGX-100 enhances Avastin + Docetaxel therapy in OVCAR-8 Ovarian Cancer Tumors



Summary

- VEGF-C is an alternate, pro-angiogenic growth factor that signals through VEGFR-2 and VEGFR-3, that may modulate sensitivity to anti-VEGF therapy and allow regrowth of tumor vasculature.
- VEGF-C is elevated in CRC patients treated with Avastin® /FOLFIRI just prior to and during disease progression.
- In several preclinical mouse models of human cancer, addition of VGX-100 to Avastin® +/- chemotherapy prolongs tumor response.
- Clinical program to co-administer VGX-100 and Avastin® to improve patient response in multiple tumor types.

VGX-100 ONCOLOGY DEVELOPMENT

Mark Sullivan
Head of Development

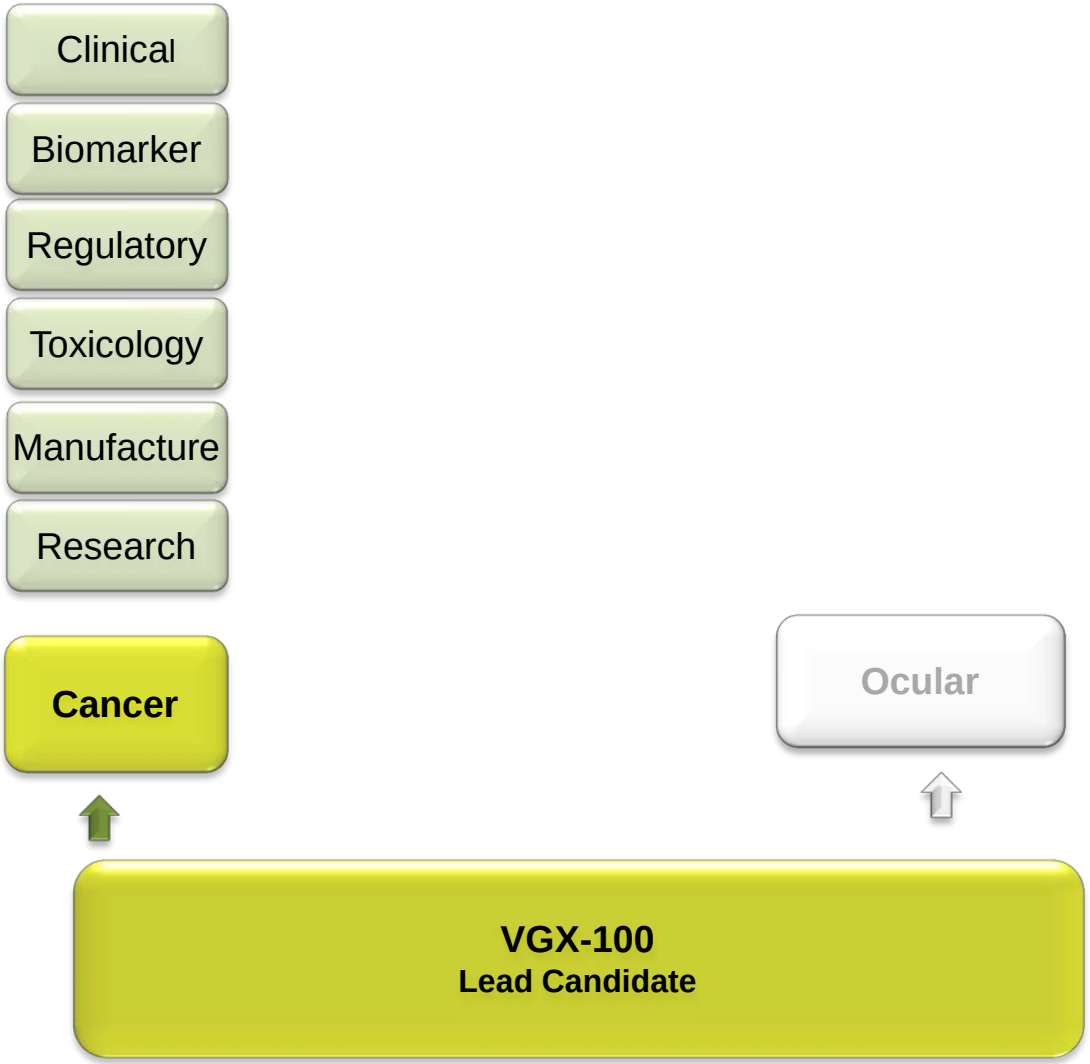
Idealised Timelines for Development of a Monoclonal Antibody in Oncology

	Pre Clinical Testing	FILE IND	Phase I	Phase II	Phase III	FILE BLA	FDA	Approval
Years	3.5		1	2	3		1.5	Total = 10-12
Test Population	Laboratory and Animal Studies		20 to 80 late stage cancer patients	100 to 300 patients with particular tumour type and chemotherapy regimen	300 to 1000 patients with particular tumour type and chemotherapy regimen		Review Process	Post Marketing Commitments and safety Monitoring
Purpose	Assess Safety and Biological Activity		Determine safety and dosage	Evaluate effectiveness, look for side effects	Verify effectiveness, monitor adverse reactions from long-term use			Large Scale Manufacturing --- Distribution --- Education
% of all new drugs that pass	50 to 100 screened		5 enter trials				1	

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

VGX-100 Oncology Product Development



VGX-100 Oncology Product Development

US-based contract research laboratory and academic collaborators

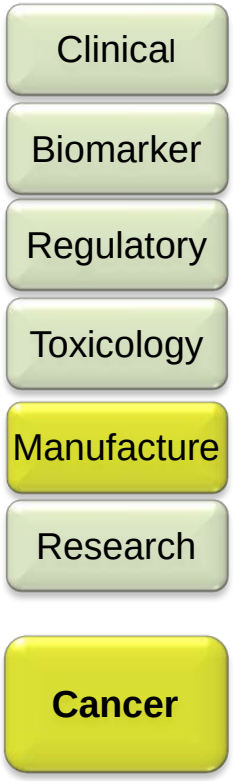
Extensive preclinical studies√

- *In vivo* and *in vitro* models√
- Optimal in combination with Avastin® and chemotherapy

Cancer

VGX-100
Lead Candidate

VGX-100 Oncology Product Development



Lonza, UK

800L clinical grade (cGMP)√

- Yield >2g/L√
- Stable formulation√

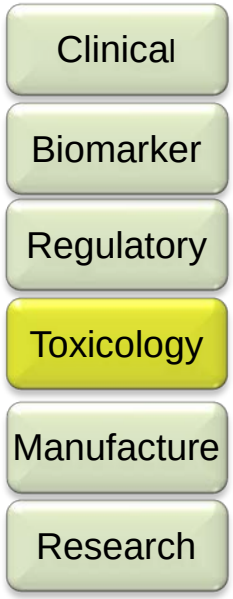
Assay development√

- Clinical√
- Preclinical√
- Manufacture release√

Research grade batch√

VGX-100
Lead Candidate

VGX-100 Oncology Product Development



Cancer

Major global toxicology laboratory

Completed according to FDA regulations√

- Pivotal toxicology studies in two species√
- Pre-toxicology “dose range finding” studies √
- Species selection √
- Pharmacokinetics in 3 species√
- Biodistribution √

VGX-100
Lead Candidate

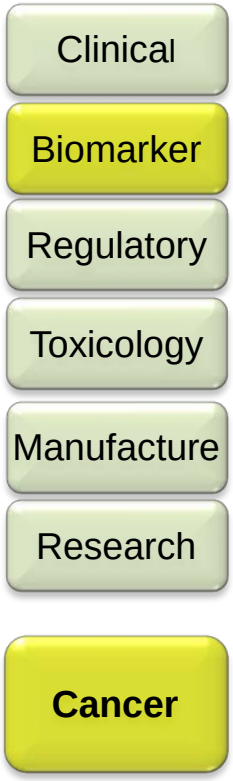
VGX-100 Oncology Product Development

Conduct under United States Food and Drug Administration Standards

Pre-IND√

IND (Q3 ‘11)

VGX-100 Oncology Product Development



Kopetz, MD Anderson

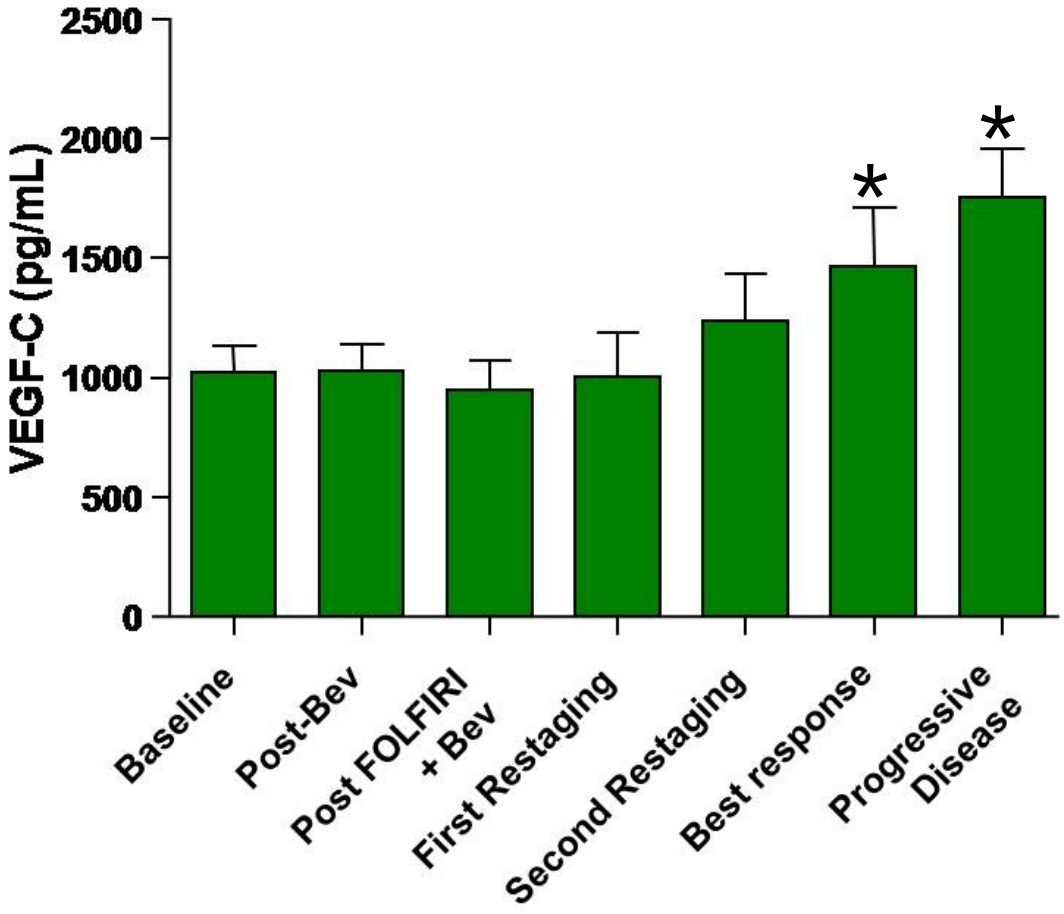
Initial clinical biomarker data√

- Repeat and expand

Program to accompany Phase I designed√

VGX-100
Lead Candidate

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



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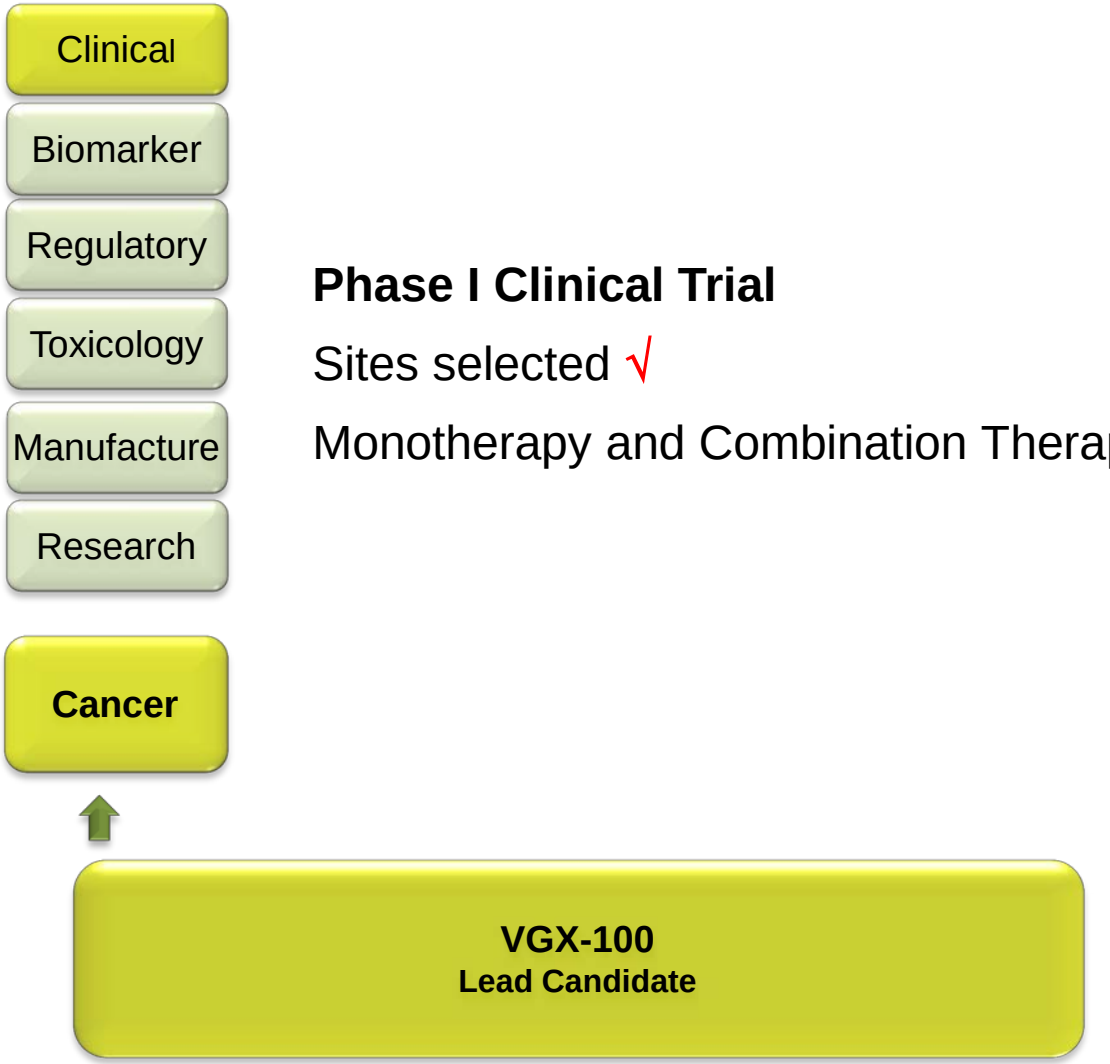
VGX-100 Oncology Product Development



Phase I Clinical Trial

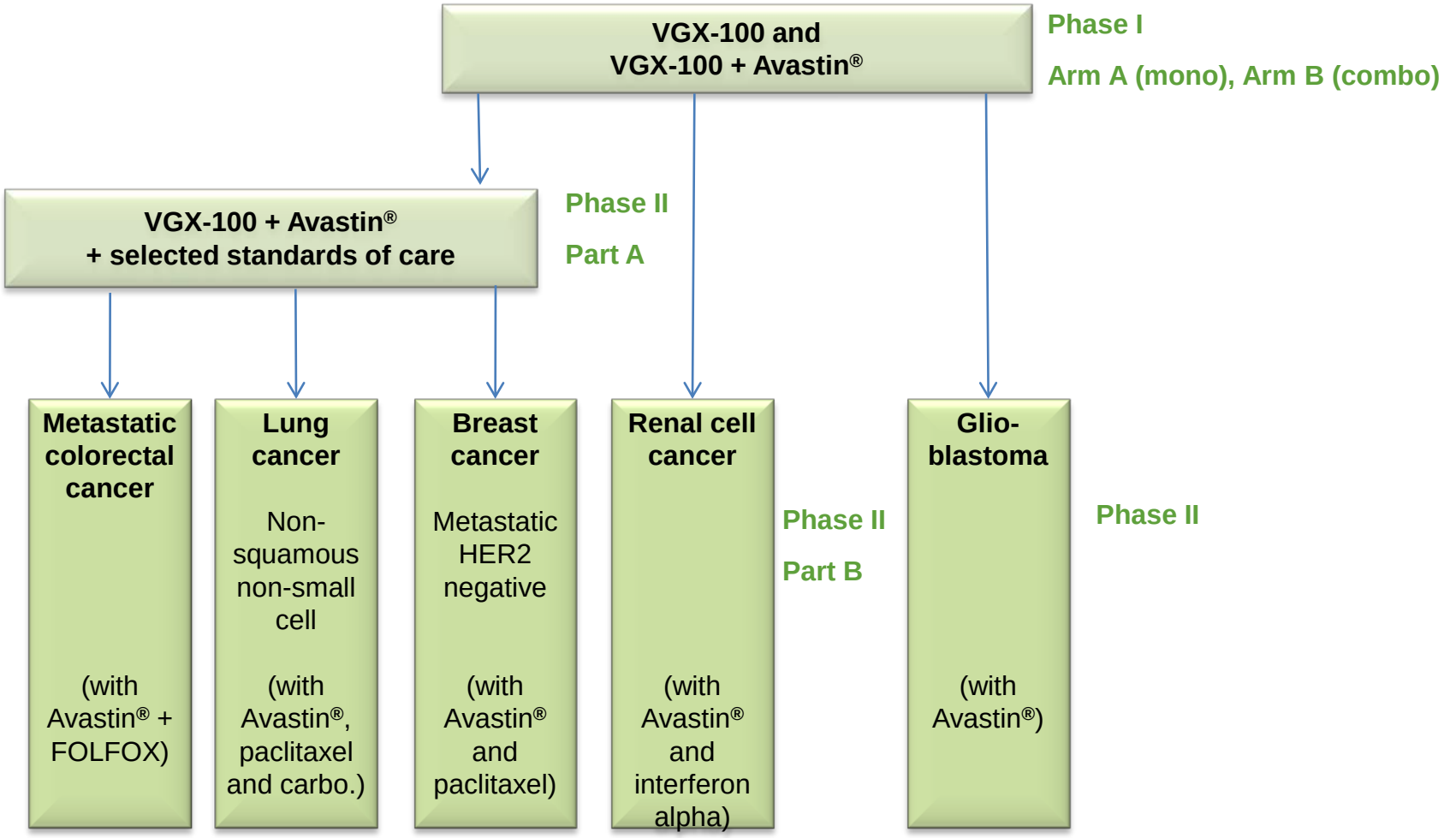
Sites selected √

Monotherapy and Combination Therapy

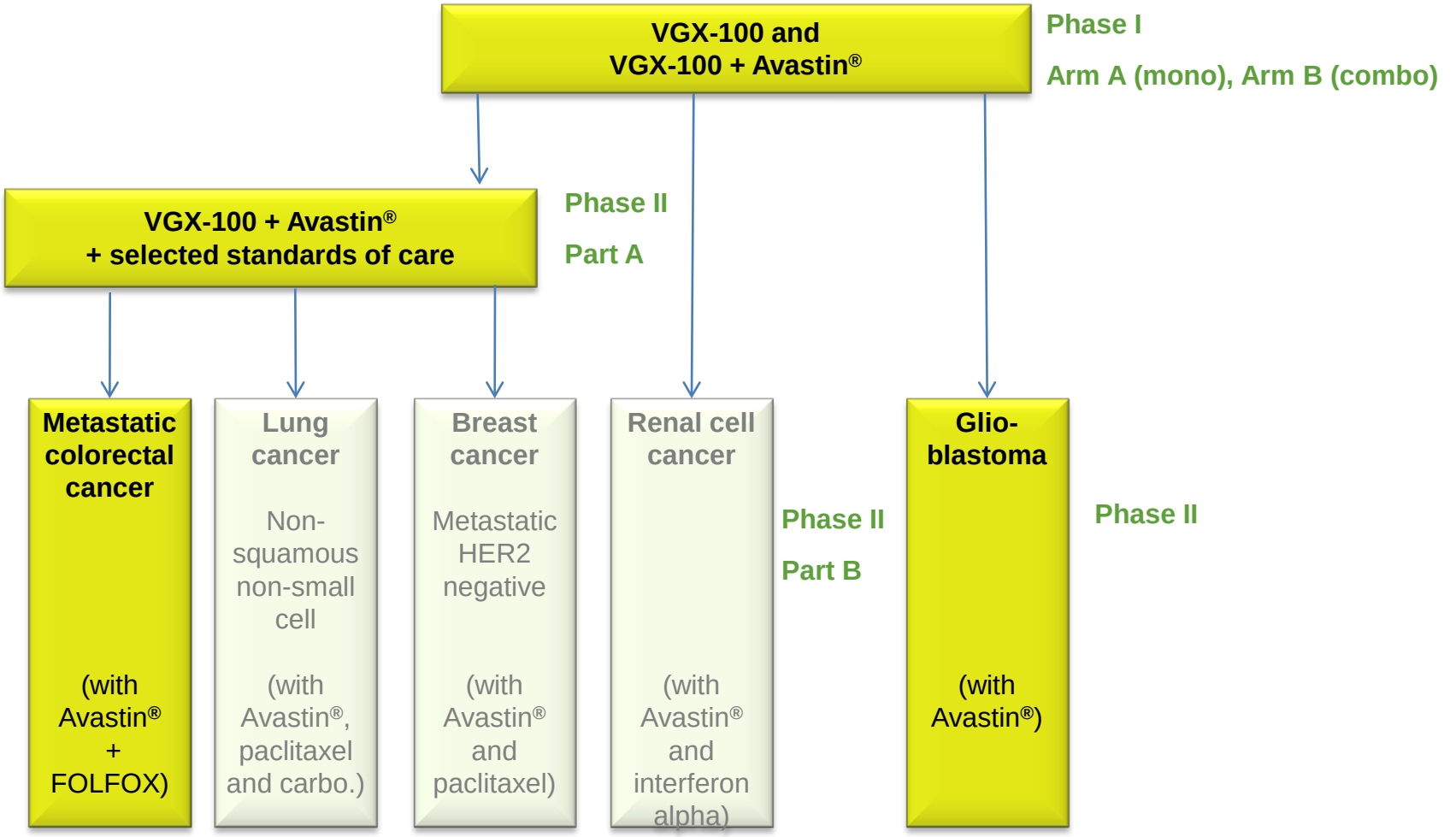
Background & Benefits of the program design

- Rapidity
  - Speed through Phase I
    - » Gain monotherapy and combination data
  - Moves quickly to homogeneous population
- Preserves options
  - Multiple cancer type
    - » Glioblastoma
      - – Important, unmet medical need
      - – Readouts are clear, fast
      - – Opportunity for accelerated registration
    - » Colorectal Cancer
      - – Significant cancer
      - – Important, unmet medical need
    - » Other

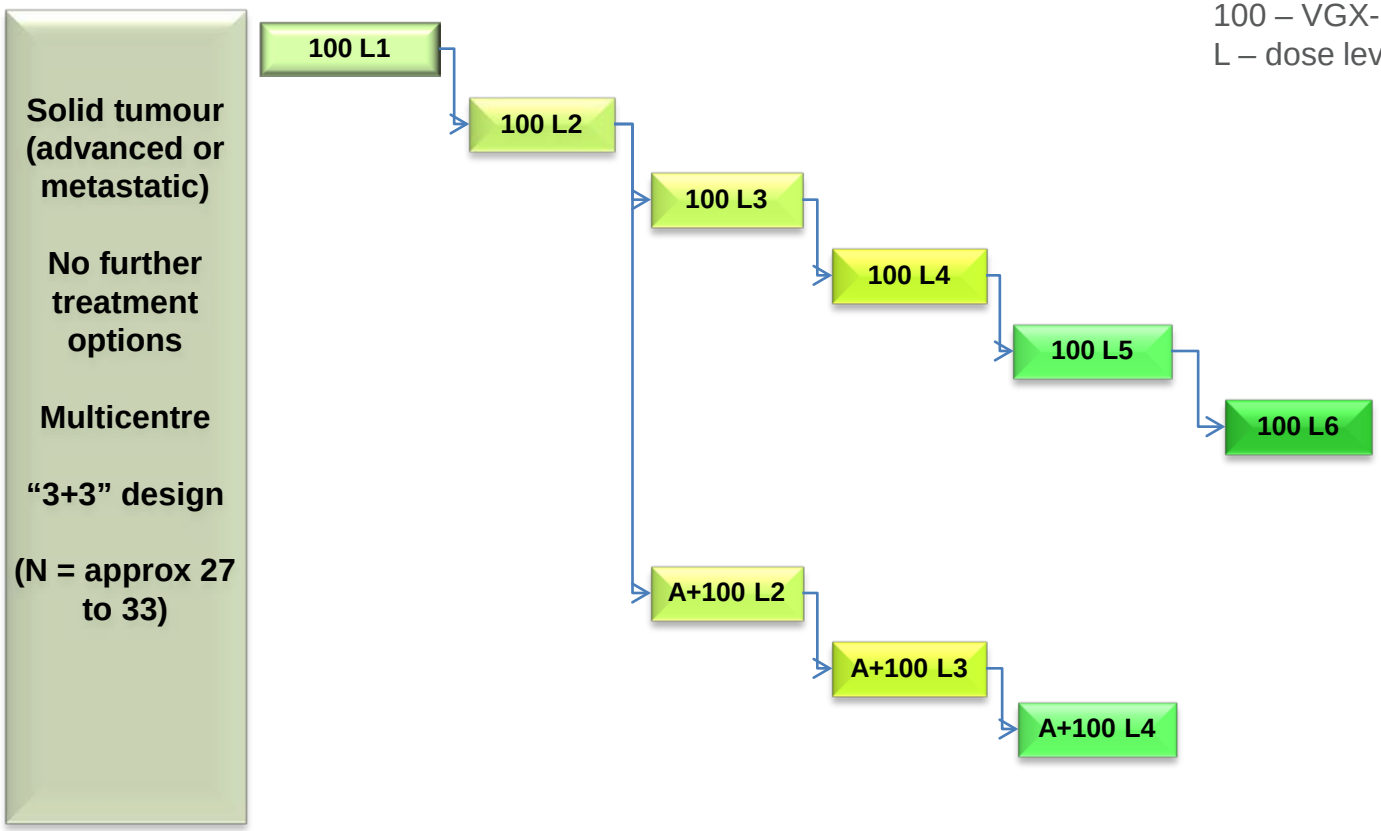
Phase I and II clinical program



Phase I and II clinical program



Phase I First-in-Human Study



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.

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

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

Avastin® Registrational Study in Metastatic Colorectal Cancer

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 3, 2004 VOL. 350 NO. 23

Bevacizumab plus Irinotecan, Fluorouracil, and Leucovorin for Metastatic Colorectal Cancer

Herbert Hurwitz, M.D., Louis Fehrenbacher, M.D., William Novotny, M.D., Thomas Cartwright, M.D., John Hainsworth, M.D., William Heim, M.D., Jordan Berlin, M.D., Ari Baron, M.D., Susan Griffing, B.S., Eric Holmgren, Ph.D., Napoleone Ferrara, M.D., Gwen Fyfe, M.D., Beth Rogers, B.S., Robert Ross, M.D., and Fairooz Kabbinavar, M.D.

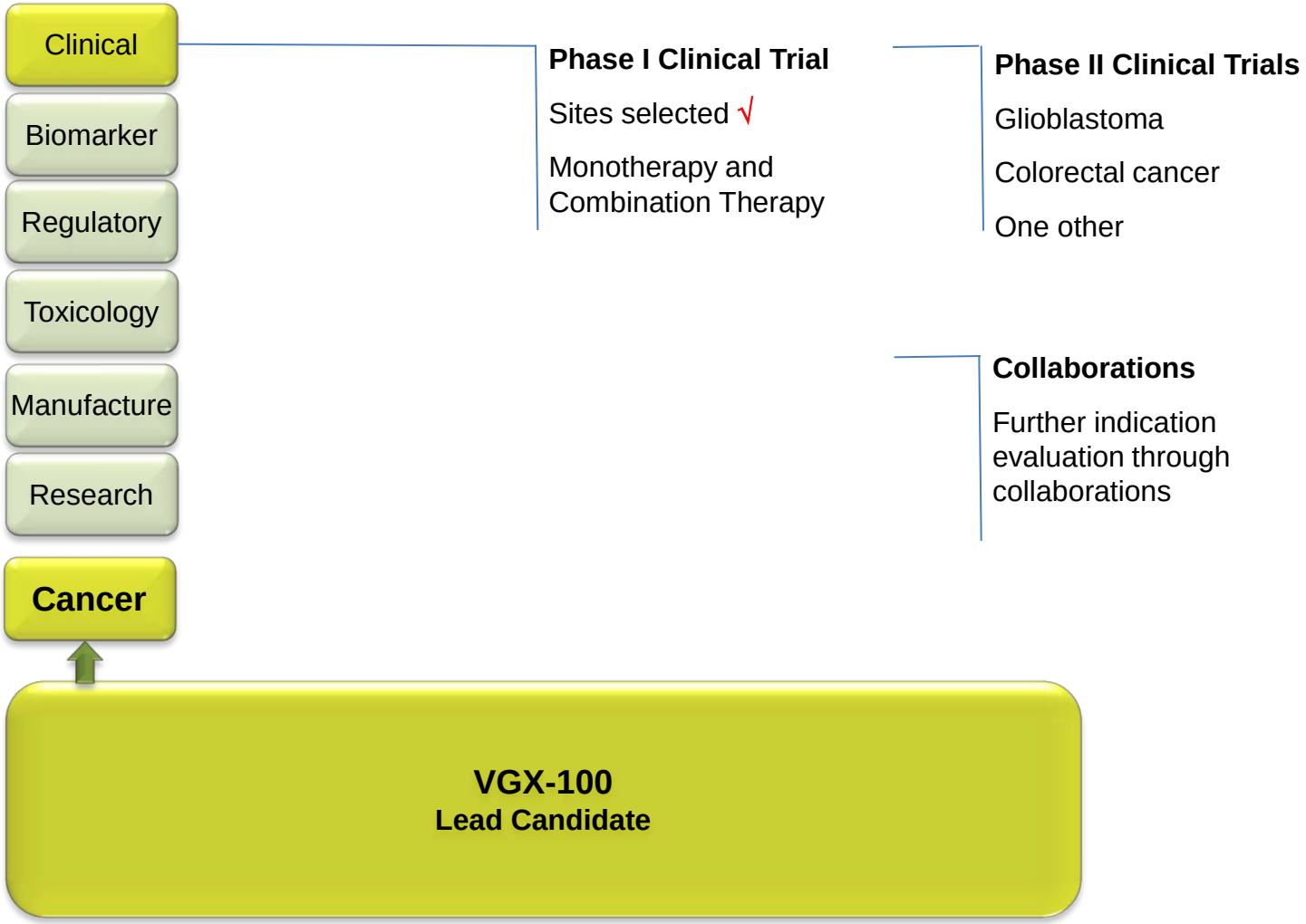
ABSTRACT

BACKGROUND

Bevacizumab, a monoclonal antibody against vascular endothelial growth factor, has shown promising preclinical and clinical activity against metastatic colorectal cancer, particularly in combination with chemotherapy.

From Duke University, Durham, N.C. (H.H.); Kaiser Permanente, Vallejo, Calif. (L.F.); Genentech, South San Francisco,

Oncology Product Development



Current Activities and Value Adding Events

Activity	Timeline
Mechanism of Action Studies	Complete
PK Studies	Complete
cGMP Manufacture	Complete
Toxicology Studies	Complete (reports awaited)
IND Filing	Q4 2011
First-in-human Clinical Study (monotherapy and in combination)	Q4 2011
Phase II studies start (Multiple Indications)	Q1 2013
Clinical proof-of-concept	2H 2014

VGX-100 OCULAR DEVELOPMENT OPPORTUNITY

Dr Megan Baldwin
Head of Preclinical R&D

circadian

The Opportunity

Leveraging the preclinical development program results in a **simplified & cost-effective** development path for VGX-100 in eye disease.

Leverage oncology program investment in:

- Conducting systemic toxicology studies
- cGMP manufacture for Ph I/II clinical trials
- Biochemical characterisation studies
- Formulation & stability studies

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

- 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 (>$500m p.a)
- Opportunity to leverage VGX-100 oncology program

Development Opportunity

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

- Initial indications:
  - **Corneal Neovascularisation (CNV)**
  - **Corneal Allograft Rejection**
  - **Dry Eye Disease**

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

- Approx. 18 – 24 months to Phase I/II

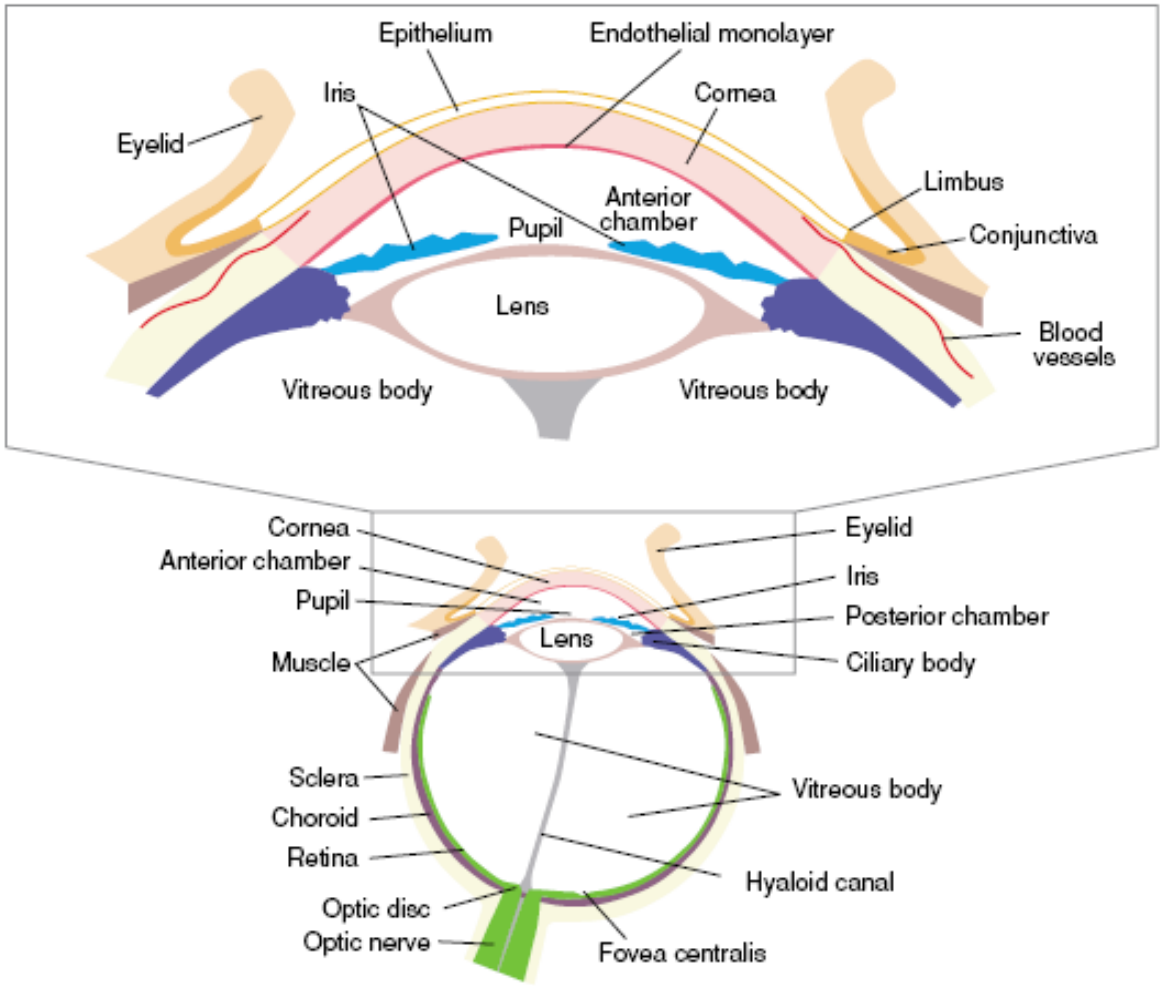
Target Product Profile in ‘Front of the Eye’ Disease

- **Indication:**
  - Administered as monotherapy, via subconjunctival injection for the treatment of:
    - Corneal neovascularisation of various aetiologies
    - ‘High-risk’ corneal allografts to inhibit graft rejection and prolong graft survival

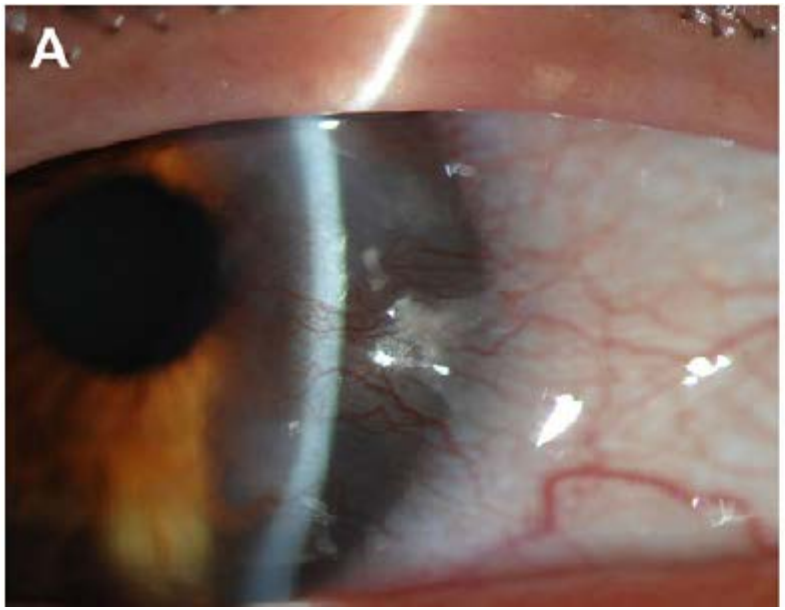
Healthy Corneas are Avascular and “Immune Privileged”

- Healthy corneas are avascular.
- Blood AND lymphatic vessels absent.
- “Immune-privileged” state: absence of vessels hinders trafficking of immune mediators between the eye and lymphoid system.

The cornea is the transparent front part of the eye that covers the iris, pupil and anterior chamber



Clinical Appearance of CNV in Inflammatory Disorders



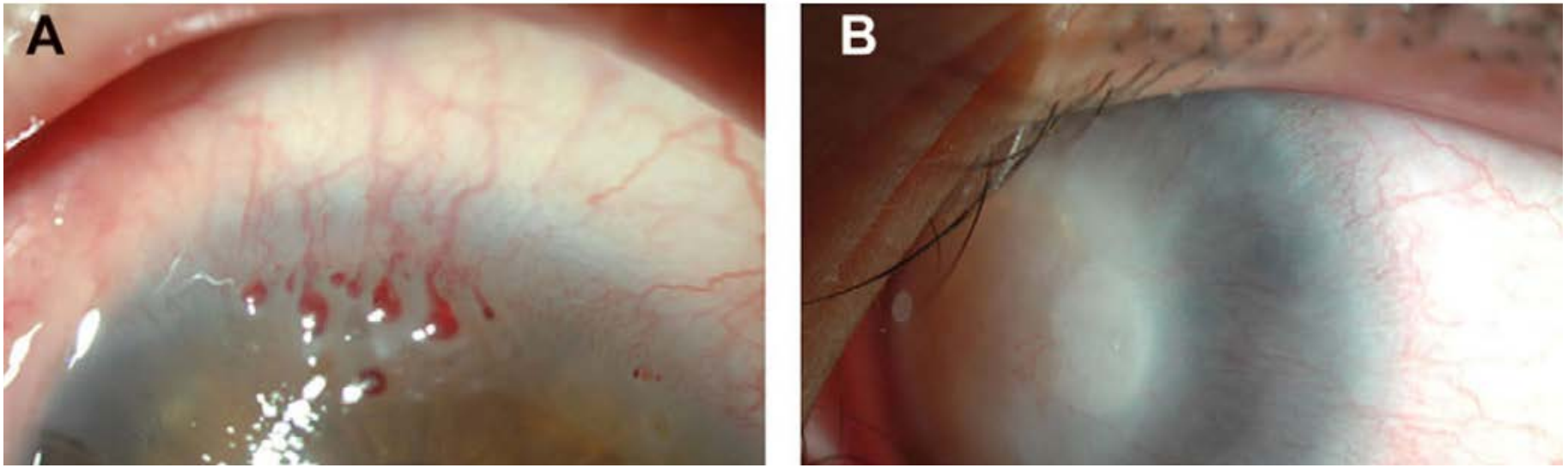
CNV in Salzmann's nodular degeneration

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

VGX-100 in Eye Disease

- VGX-100 may have clinical utility in a **broad range** of eye diseases and pathologies that are characterised by:
  - aberrant or increased neovascularisation
  - inflammation, and
  - alloimmunity.

eg. **Chronic dry eye:** complex immune mediated disorder characterised by lymphangiogenesis without hemangiogenesis, affecting 5 million people over 50 yrs of age in the US.
Keratitis: corneal inflammation,
Alkali/acid chemical injury,
Aphakic Bullous Keratopathy: corneal edema from cataract extraction

Corneal Neovascularisation

Expert Roundtable Outcome: Consensus Statements on Corneal Neovascularisation

"[There are] several very serious unmet medical needs in the treatment of corneal neovascularisation (CN) with underlying corneal diseases.

We anticipate that the anti-angiogenic strategy will become an integral part of the treatment regimen to address the unmet medical needs in the field of CN and to avoid the dramatic complications of CN."

Corneal Neovascularisation

- CNV is a common and non-specific response to a variety of ocular insults, for example:
  - Infection (ocular herpes simplex)
  - Trauma (surgery, burns)
  - Diseases & immunological conditions (LSCD)
- Scarring, oedema, lipid deposition, persistent inflammation that affects visual acuity and may cause blindness.
- Significant risk factor for corneal allograft rejection.

- Insult upregulates growth factors leading to angiogenesis & lymphangiogenesis.
- Vessels grow into cornea from limbus.

Common Mechanism of CNV

- VEGF/VEGFR pathway implicated as key driver of angiogenesis and lymphangiogenesis in CNV originating from various causes.

- **Rationale for VGX-100 for treatment of CNV:**

  - Block VEGF-C mediated activation of VEGFR-2 to reduce angiogenesis
  - Block VEGF-C mediated activation of VEGFR-3 to reduce angiogenesis and lymphangiogenesis
  - Inhibit inflammation and Antigen Presenting Cells into cornea

Need for Non-Steroid Based Treatment of CNV drives LARGE Market Opportunity

Treatment

- Corticosteroids to control inflammation (significant risks, little direct affect on angiogenesis, infections must be resolved before treatment)
- Need for non-steroid based treatments

Market Opportunity

- Large (estimated prevalence of CNV in 4-5% of all pts presenting to eye clinics)
- Potential for concurrent use with corticosteroids

Corneal Transplantation

Corneal Transplantation

- Multiple reasons/indications necessitating corneal transplantation.
- ~40000 corneal transplants performed per yr (US)
- ~25% are ‘high risk’ (vascularised corneal bed).

- Uncomplicated first grafts have a >90% success rate.
- Risk of graft failure increases to 50-90% if the recipient corneal graft ‘bed’ is vascularised.
- Graft failure involves blood and lymphatic mediated mechanisms.

Existing & Supportive Preclinical Data:

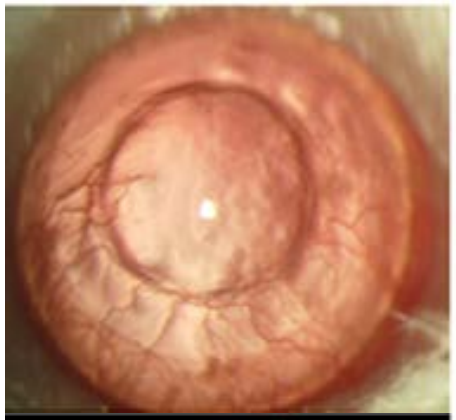
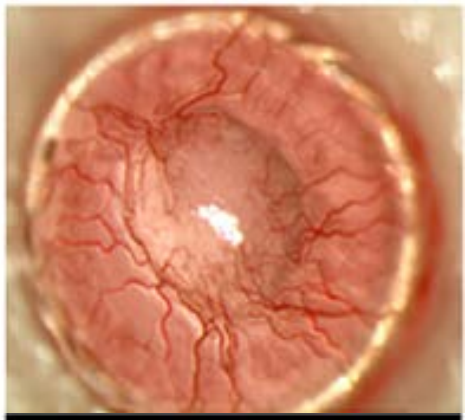
VGX-100 improves Corneal Transplant Survival

VGX-100 improves corneal transplant survival *(collaboration with Harvard Uni., Schepens Eye Institute)*

- Preclinical data demonstrating efficacy of VGX-100 in extending period of corneal graft survival (ie. inhibiting corneal graft rejection).
- VGX-100 administered systemically via IP injection (20 mg/kg day prior to injection, every alternate day for 2 weeks).
- Data presented at ARVO 2010 and manuscript submitted.

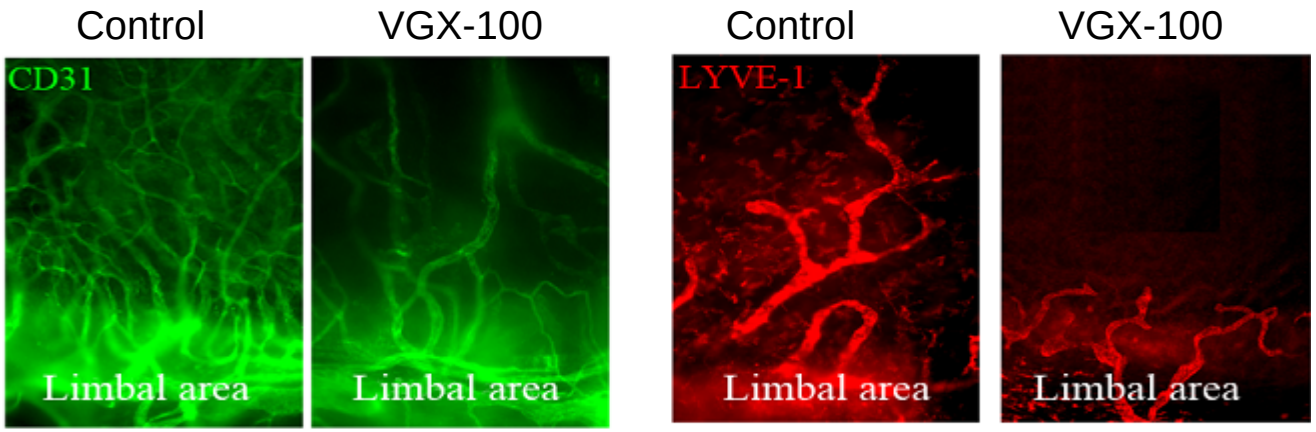
Rejected corneas are infiltrated by blood and lymphatic vessels and over-express VEGF-C and VEGFR-3

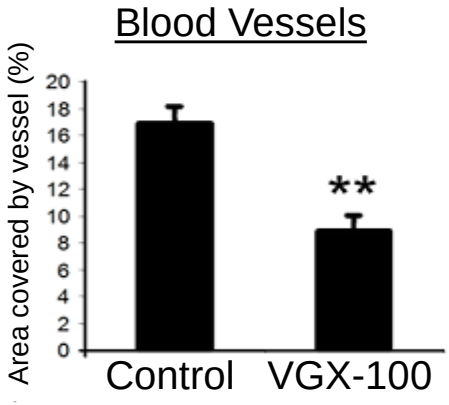
Transplanted Corneas: 3 wks Post-Transplant

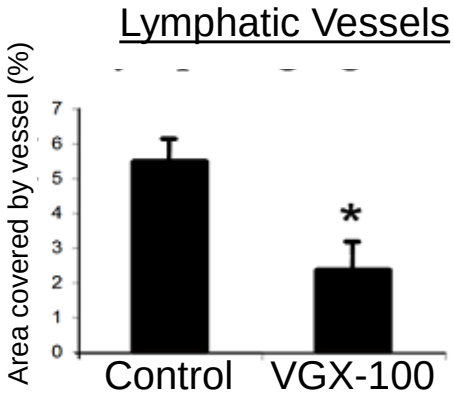
	ACCEPTED	REJECTED
Photomicrographs		
Flat-mount IHC stained corneas: **LYVE-1** (lymphatics) **CD31** (blood vessels)		

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

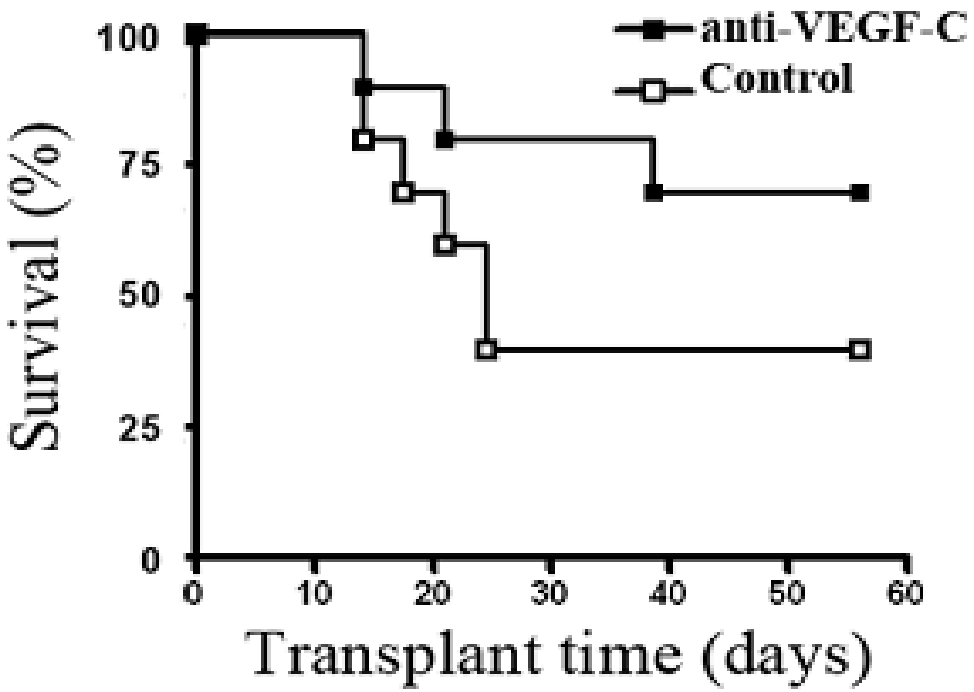






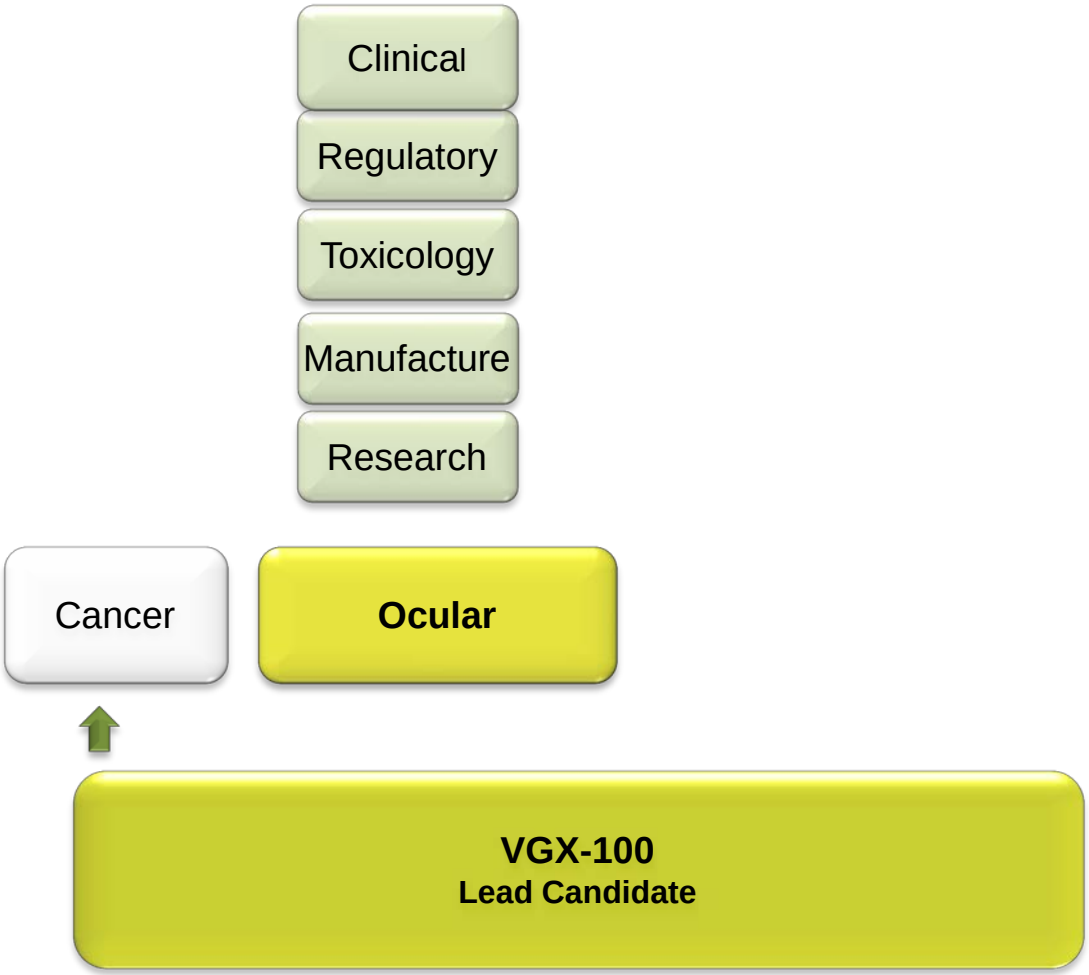
Day 7 post-transplant

VGX-100 Promotes Corneal Transplant Survival

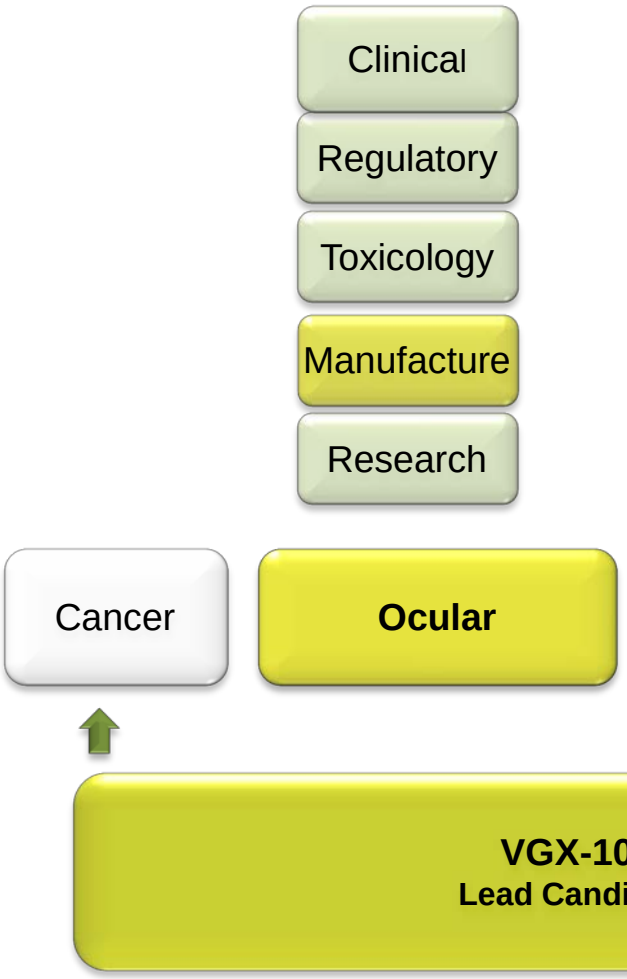


ARVO Annual Meeting 2010. Program#/Poster#1554/D995

VGX-100 Ocular Product Development



VGX-100 Ocular Product Development



Lonza, UK

800L clinical grade (cGMP)√

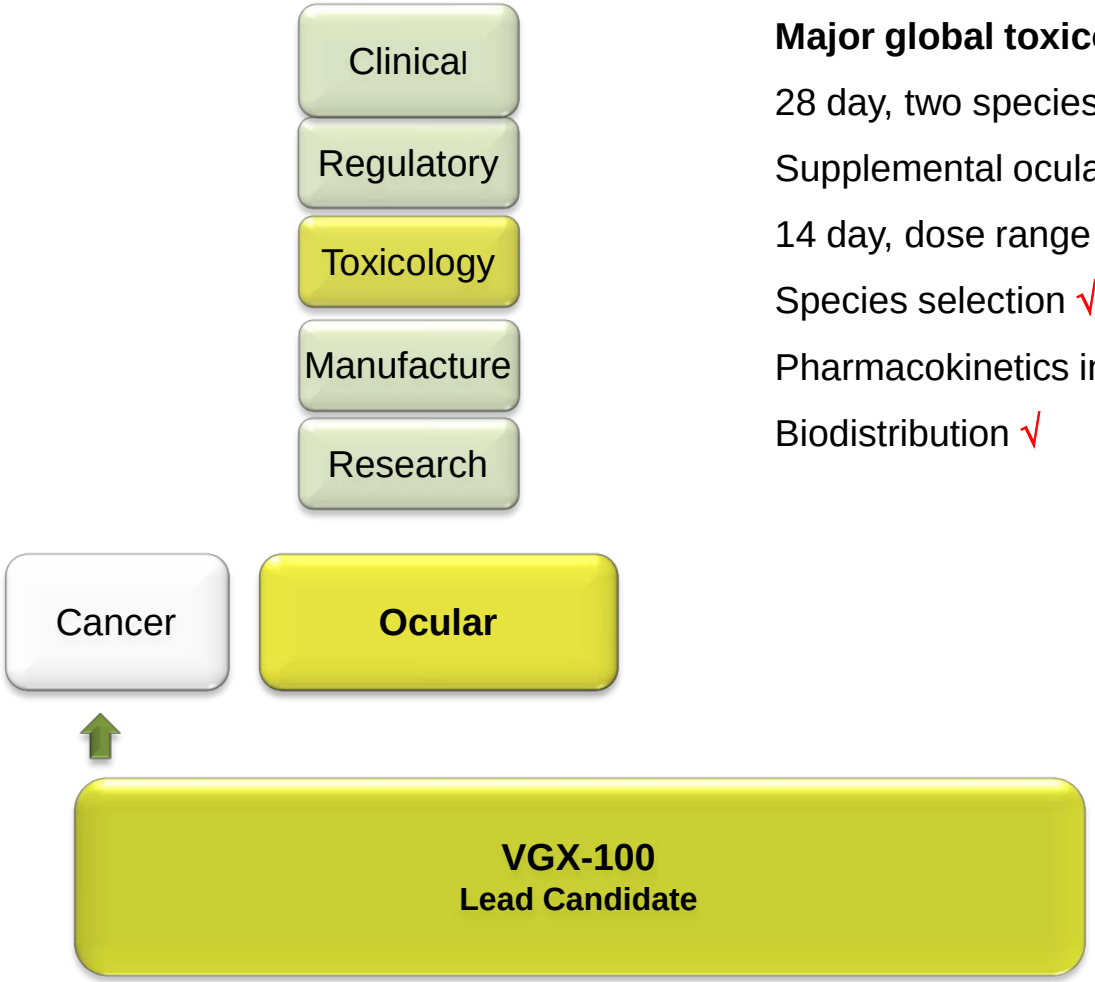
- Yield >2g/L√
- Stable formulation√

Assay development√

- Clinical√
- Preclinical√
- Manufacture release√

Research grade batch√

VGX-100 Ocular Product Development



Major global toxicology laboratory

28 day, two species √

Supplemental ocular toxicology studies

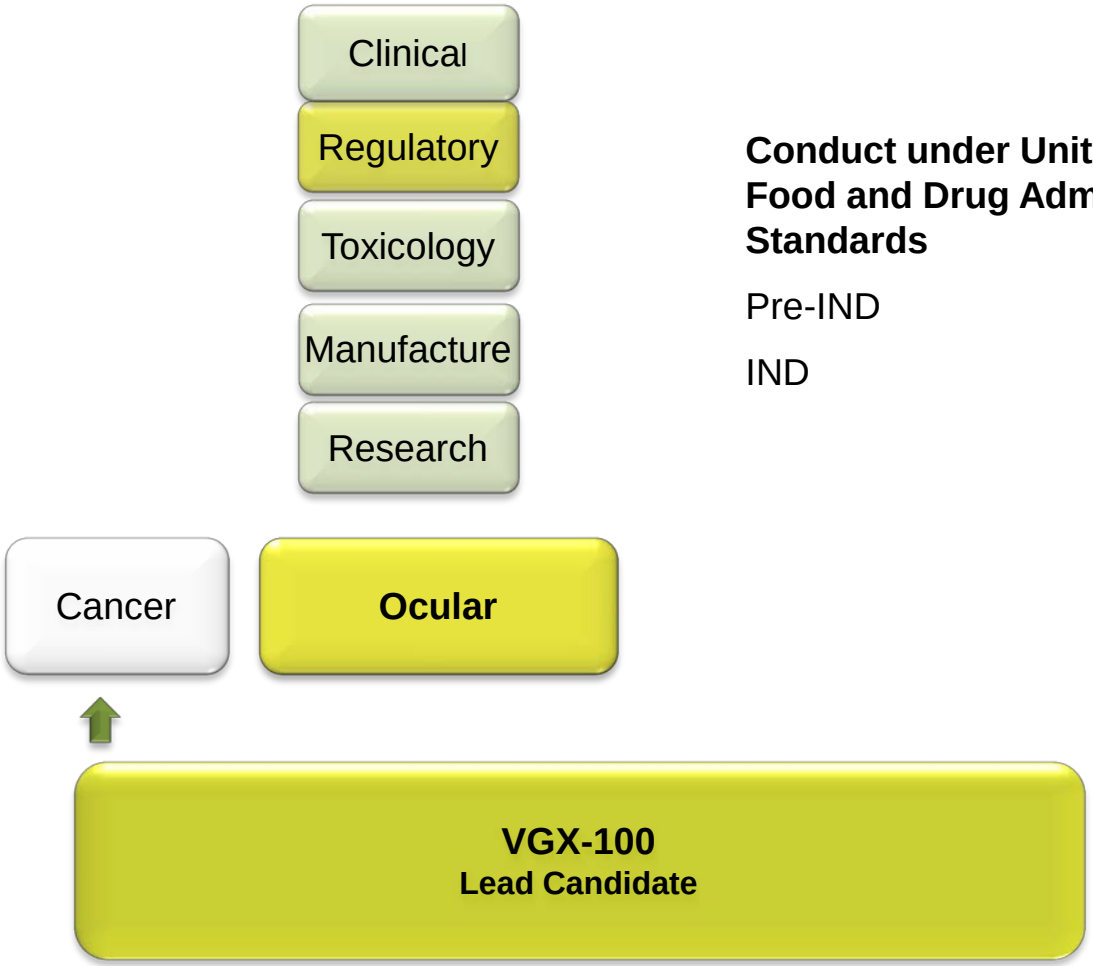
14 day, dose range finding studies √

Species selection √

Pharmacokinetics in 3 species √

Biodistribution √

VGX-100 Ocular Product Development

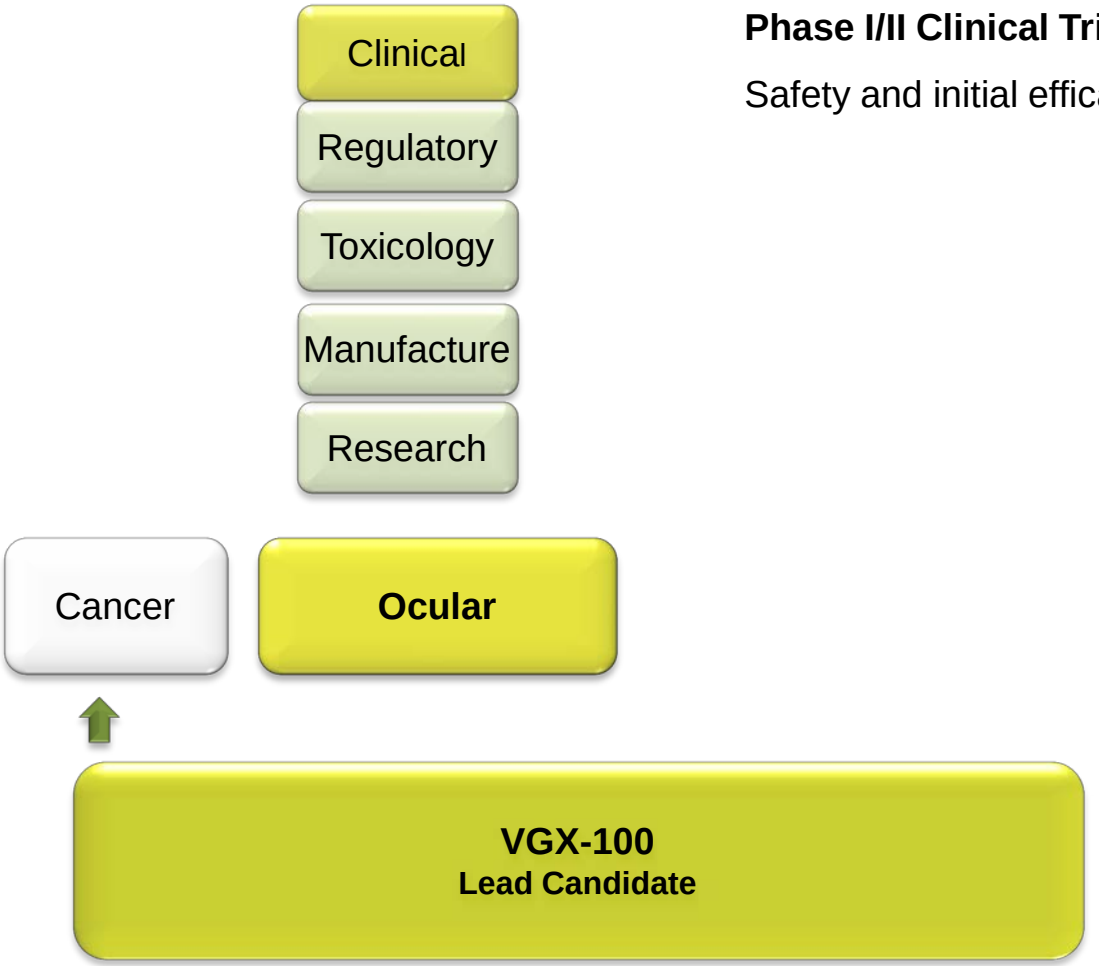


Conduct under United States Food and Drug Administration Standards

Pre-IND

IND

VGX-100 Ocular Product Development



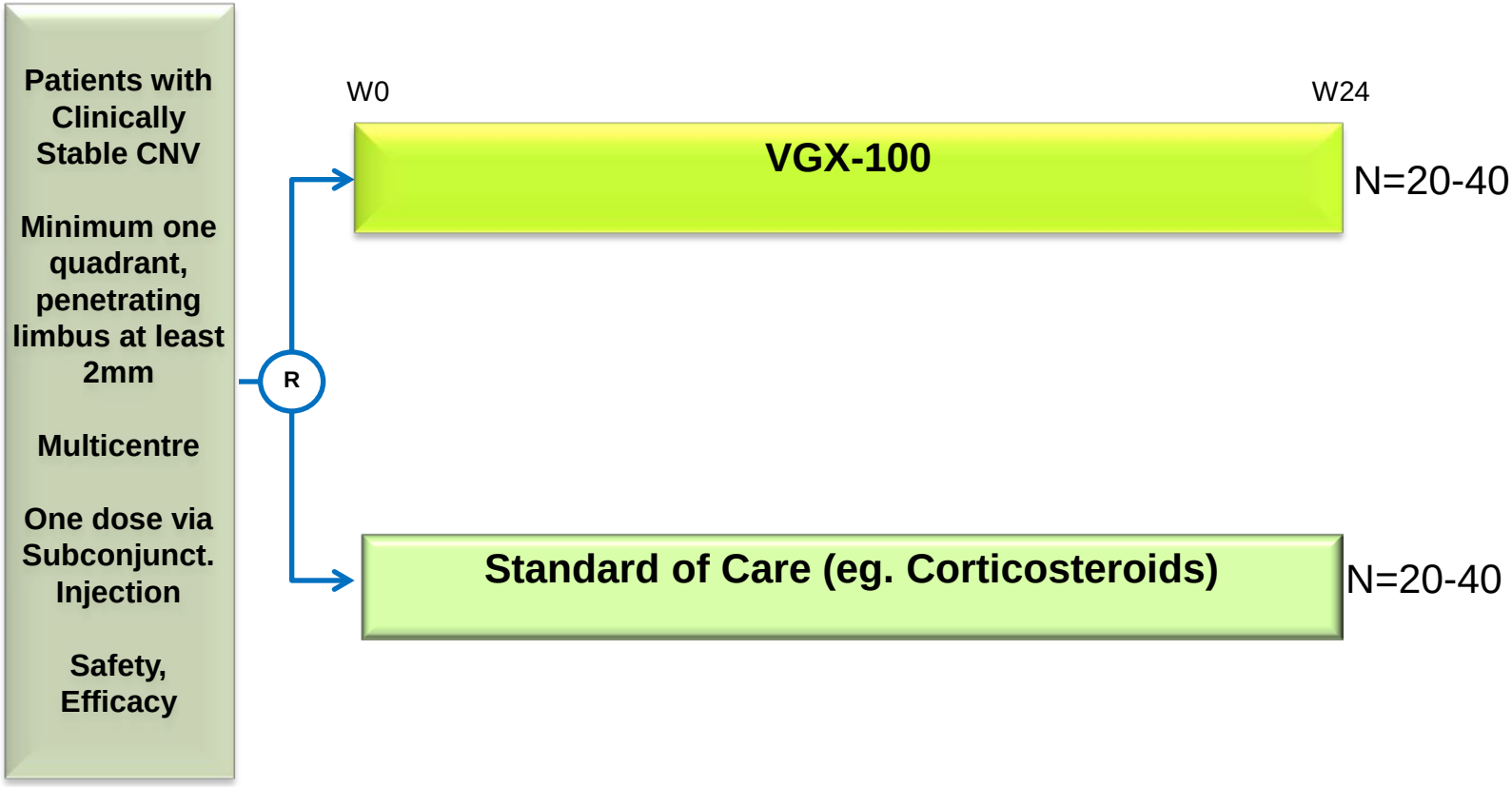
Phase I/II Clinical Trial

Safety and initial efficacy in 1st trial

Clinical Studies: Likely trial design

- Phase I/II dose escalation: safety, PK, efficacy (PhII)
- Patients with clinically stable CNV (minimum one quadrant, penetrating over limbus at least 2mm).
- One dose of 0.1cc subconjunctival VGX-100
- Ophthalmological examinations at 1 day, 1 wk, 2 wks,3 wks, 1 mo, and monthly thereafter.
- Evaluate. May undergo repeat dose at 3 mos.
- Primary Outcome Measures: Regression of CNV (Slit-lamp photographs, fluorescein angiograms.)
- Secondary Outcome Measures: Safety monitoring, visual acuity.
- Timeframe: Phase I: 6-9 months; Phase II: 12-18 months

Phase II:
VGX-100 for Treatment of Corneal Neovascularisation



Ophthalmological Examinations: day 1, 1 wk, 2wks, 3 wks, 1 month, monthly thereafter.
Primary Outcome Measures: Evaluation of CNV regression by fluorescein angiography.
Secondary Outcome Measures: Safety monitoring, visual acuity

Current Activities and Value Adding Events

ACTIVITY	TIMELINE
Further efficacy data in preclinical CNV & CT 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

Wrap Up

Robert Klupacs
Chief Executive Officer

3 years on…

- VGX-100 to achieve major milestone of IND in next few months
- VGX-100 to commence Phase 1 clinical trials Q4 2011
- VGX-100 Phase 2 data in oncology by second half of 2014
- New major opportunity for VGX-100 in front of eye disease with initial clinical data by H1 2014
- Ongoing scientific validation for role of VEGF-C in various diseases

3 years on…

- One product in the clinic – IMC-3C5 being developed by Eli Lilly
- A VEGF-D diagnostic on the market for LAM
- A cancer diagnostic for CUP close to being launched by Healthscope
- Superb group of internal and external scientific and development professionals
- Approx $25M in cash and investments

Appendix

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