Annual General Meeting

November 18 2014

Megan Baldwin , PhD

CEO & Managing Director

Circadian Technologies (ASX:CIR, OTCQX:CKDXY)

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Corporate Achievements

Corporate

- ✓ Restructure to focus on ophthalmology
- ✓ A$17.4m capital raising
- ✓ A$2.5m R&D tax rebate (2012-13) on local & international R&D expenditure

Program Achievements

Opthea

- ✓ OPT-302 designated lead program
- ✓ Signed cell line commercial license agreement
- ✓ Presented OPT-302 data at international ARVO conference
- ✓ Completed Pre-IND meeting
- ✓ Commenced IND-enabling GLP safety/toxicology studies
- ✓ Advanced OPT-302 manufacturing
- ✓ Successful grant application for OPT-302 manufacture
- ✓ Allowed key US patent for VEGFR-3 Traps

Ceres

- ✓ Completed Phase 1a/1b oncology clinical trial
- ✓ Selected to present clinical data at international ASCO conference
- ✓ Phase 2 ready

Capital Raising – Key Objectives

Accelerate development of lead compound OPT-302

- Scale-up & manufacturing of OPT-302 for clinical programs
- Complete US IND filing
- Initiate Phase 1 dose escalation trial in combination with Lucentis® in Wet Age-related Macular Degeneration (wet AMD) patients
- Advance OPT-302 through Phase 2a clinical studies in wet AMD
- Generate additional clinical & preclinical data to fully establish the profile of OPT-302 in wet AMD & other eye diseases

R&D and Business Development

- Complete data analysis of Phase 1 clinical program for VGX-100 in solid tumours
- Advance business development to accelerate licensing opportunities for VGX-100
- Improve balance sheet to provide a strong position for partnering opportunities

Capital Raising Overview

- Transformational $17.4m capital raising completed
- Expected to fund Circadian through Q4 2017
- $0.175 per share comprising
  - Placement of A$14m
  - Fully underwritten 2 for 5 non-renounceable Rights Issue raised $3.4m
- 1 free attaching option for every 2 shares subscribed for under the Offer
  - Exercisable at $0.27 at any time before expiry on 25 November 2018
- Managed & underwritten by Bell Potter
- Solid uptake of shares by existing investors in Rights Issue
  - 53% uptake of shares held by eligible shareholders
  - 44% of total shares on offer
- Strong support from institutional & sophisticated investors in the US, Europe & Australia
- Validates CIR technology and strategy to advance OPT-302 to clinical milestones

Financial Position Post-Capital Raise (Nov 25 2014)

– Ticker Symbol:	ASX: CIR, OTCQX: CKDXY
– Share Price:	A$0.17 (as at Nov 18 2014)
– Total Shares on Issue	148,086,328
– New Options on Issue	49,726,669
– Market Capitalisation	A$25.2m
– Trading Range	A$0.16 – 0.255 (last 12 months)
– Top 10 Shareholders Own	68%
– Cash	A$20.5m
– Listed Investments	~A$1.7m

Overview

Leader in VEGF-C/-D and VEGFR-3 targeting compounds in ophthalmology and oncology

- Extensive worldwide intellectual property platform in respect of VEGF-C, VEGF-D and VEGFR-3
- Lead compound OPT-302 blocks VEGF-C & VEGF-D
- OPT-302 expected to enter Ph 1 clinical trial for wet AMD
  - Phase 1 clinical trial expected to commence 2Q15
  - Results from Phase 1 clinical trial expected 1Q16
  - Results from Phase 2a clinical trial expected 2Q17
- VGX-100 Phase 1a/b study completed enrolment
  - Phase 2 ready asset poised for licensing/partnership
- Eli Lilly partnered compound IMC-3C5 to complete Phase 1 in solid tumours in 1H15
- Strong management team with experience in developing drugs targeting the VEGF pathway, wet AMD and oncology

Program Update
OPT-302 for Wet AMD

Lead Program
OPT-302 for Wet AMD

Lead molecule:

- OPT-302 (soluble VEGFR-3, VEGF-C/-D 'Trap')

Mechanism:

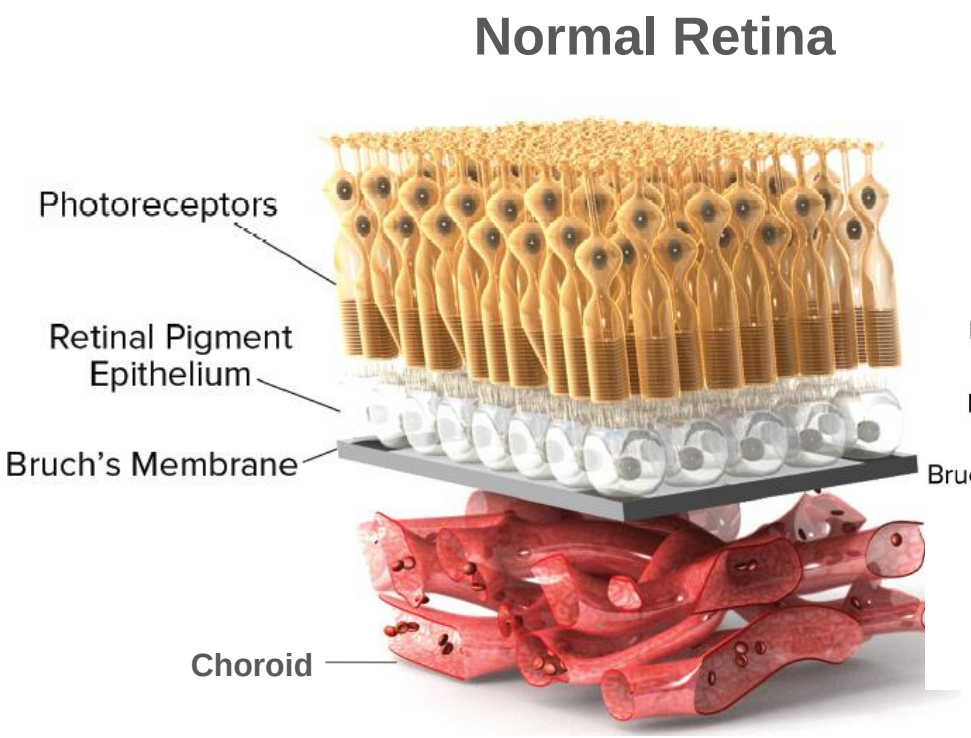
- Blocks VEGF-C and VEGF-D:
  - Inhibits blood vessel growth
  - Inhibits vessel leak

Strategy:

- To develop OPT-302 for use in combination with existing VEGF-A inhibitors for the treatment of wet AMD
- Achieve complete blockade of the VEGF pathway

OPTHEA circadian

The normal retina and ‘wet’ (neovascular) AMD



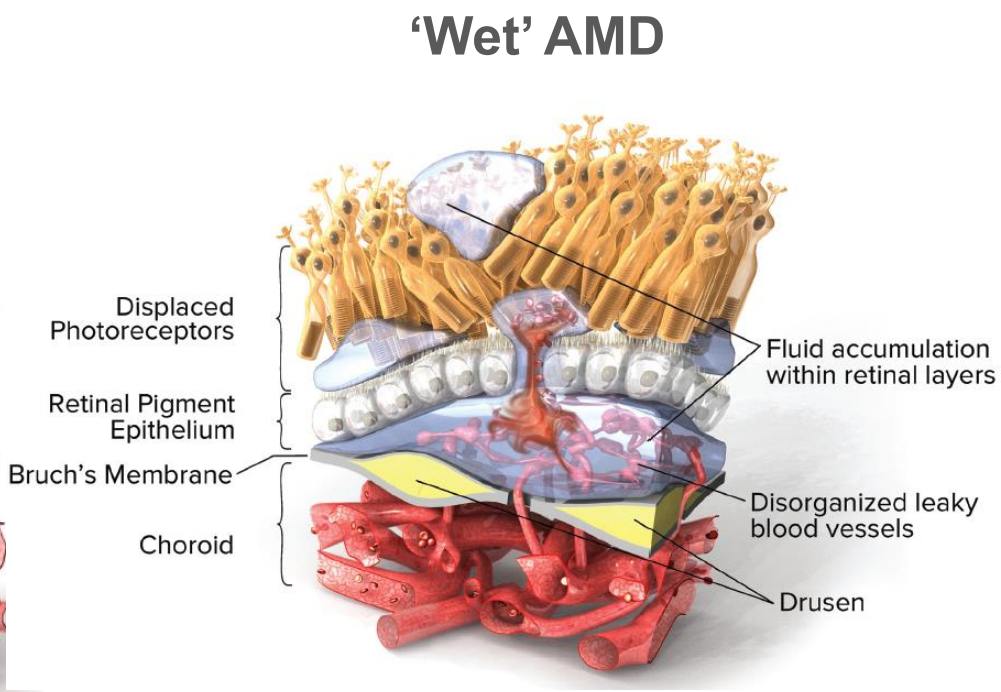


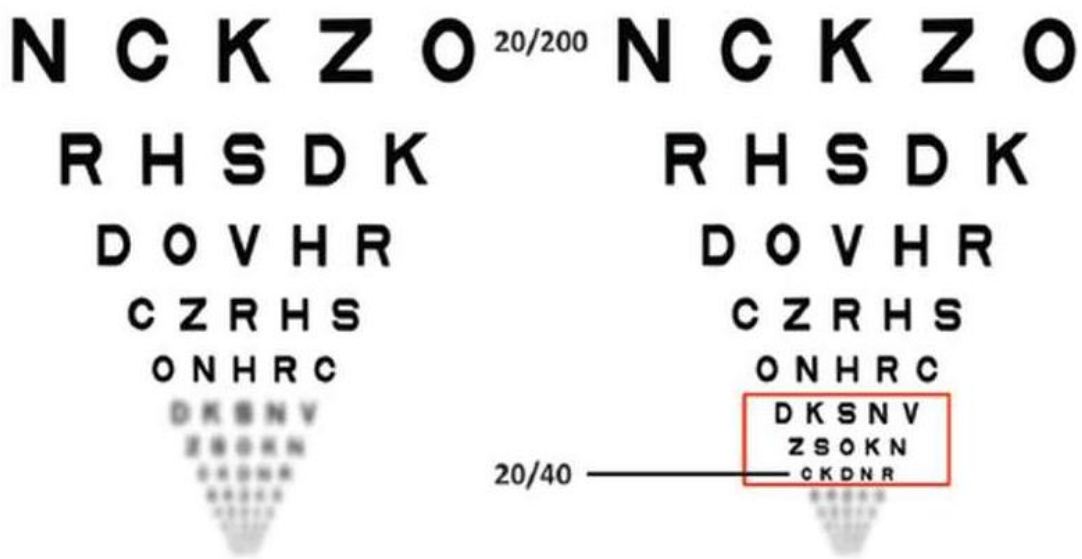
Figure: The Angiogenesis Foundation

Wet (neovascular) AMD

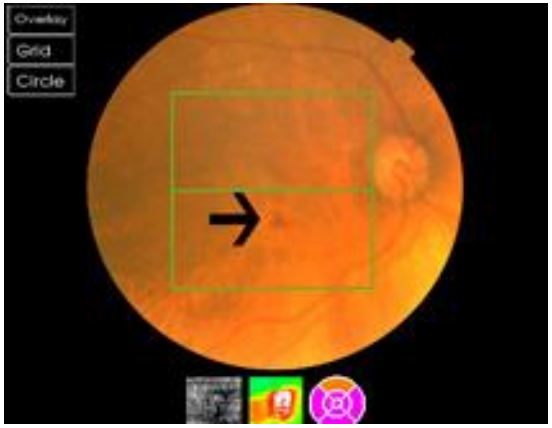
Photo: The Angiogenesis Foundation

Routine Non-Invasive Monitoring Procedures for Disease and Treatment Efficacy

Eye Chart *(Visual Acuity)*



Retinal Image



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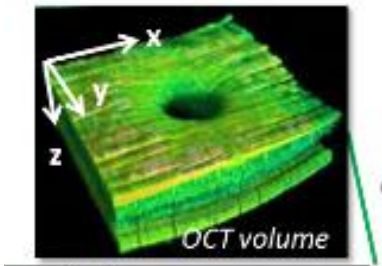
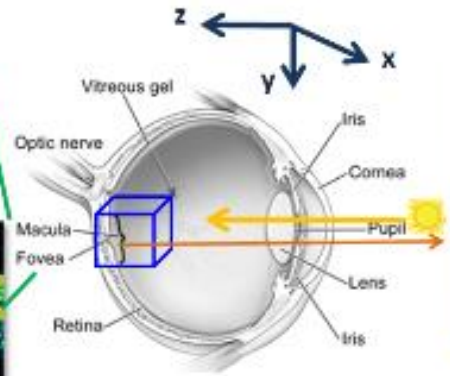
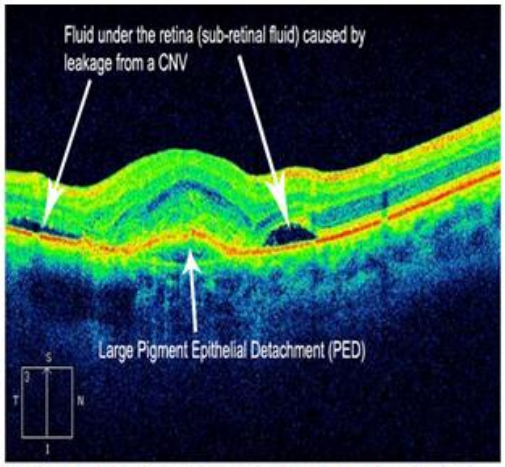
Routine Non-Invasive Monitoring Procedures for Disease and Treatment Efficacy

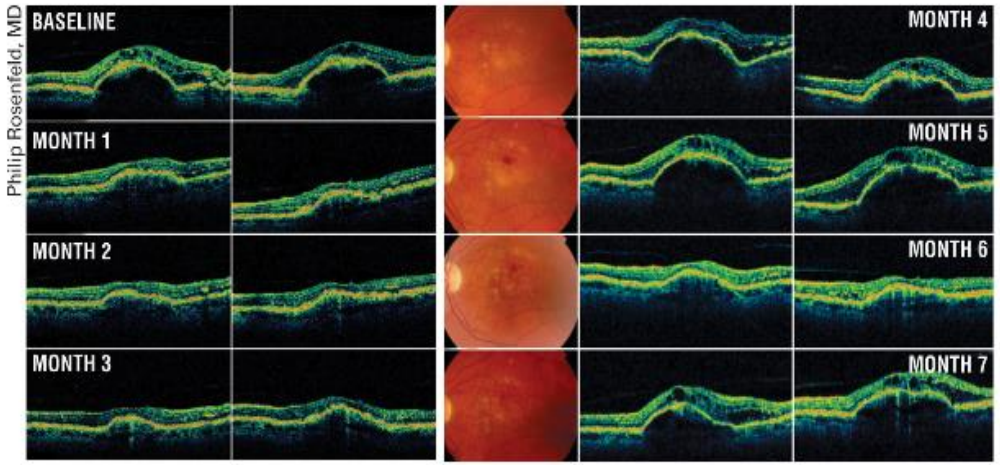
OCT(*Optical Coherence* Tomography
(Fluid, hemorrhage, retinal thickness, retinal detachment)







OCT image showing wet macular degeneration



OPTHEA circadian

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 >$US5B p.a. market opportunity in wet AMD in US alone
- Increasing with aging population

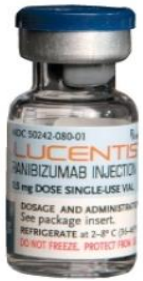
- Only two targeted therapies approved for wet AMD
- Both target VEGF-A
  - Roche/Novartis: **Lucentis®**
  - Regeneron/Bayer: **Eylea®**
  - Roche/Genentech: **Avastin®** (off-label)

The opportunity for OPT-302: An unmet medical need remains despite anti-VEGF-A therapy

- VEGF/VEGFR pathway recognised as most important pathway for blood vessel growth and vessel leakage
- Existing therapies target VEGF-A but not VEGF-C or VEGF-D

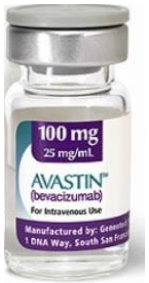
- Long-term single-agent anti-VEGF-A therapy (Lucentis®/Eylea®) results in a suboptimal visual outcome
  - >50% of patients do not experience a significant vision gain
  - Phase III trial results indicate that between 50-70% patients have retinal fluid despite anti-VEGF-A therapy
- Combined VEGF-A/VEGF-C inhibition has the potential to improve patient response by **more complete** blockade of blood vessel growth & vessel leakage

More complete blockade of the VEGF/VEGFR pathway is clinically more effective than anti-VEGF-A therapy



Wet AMD

Improved efficacy of Lucentis® that blocks all isoforms of VEGF-A compared to Macugen® that selectively blocks the VEGF-A_{165} isoform

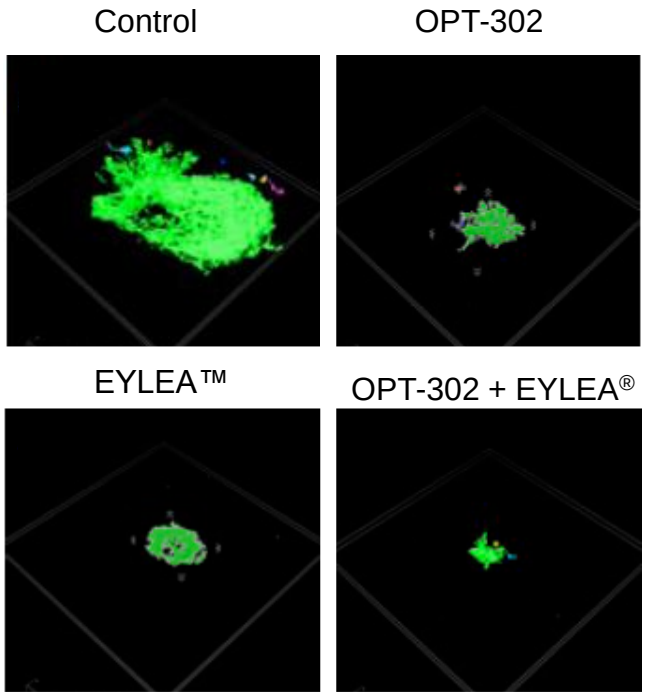


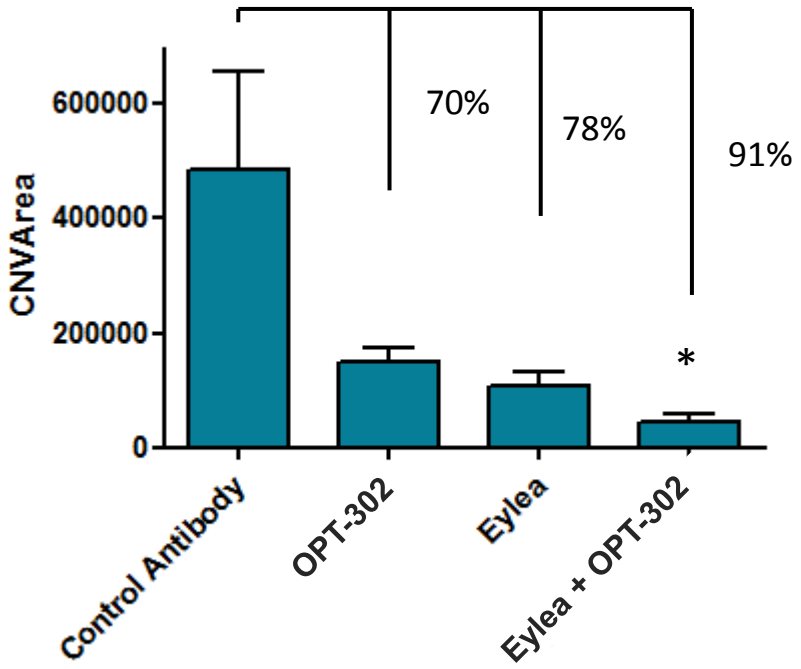
Gastric Cancer

Cyramza® (neutralising VEGFR-2 that blocks VEGF-A, VEGF-C and VEGF-D) is more effective than Avastin® (selective VEGF-A inhibitor) in gastric cancer

Significant additive activity of OPT-302 & Eylea® in mouse AMD

Combined inhibition of VEGF-A (Eylea®), VEGF-C and VEGF-D (OPT-302) is more effective than inhibition of VEGF-A alone



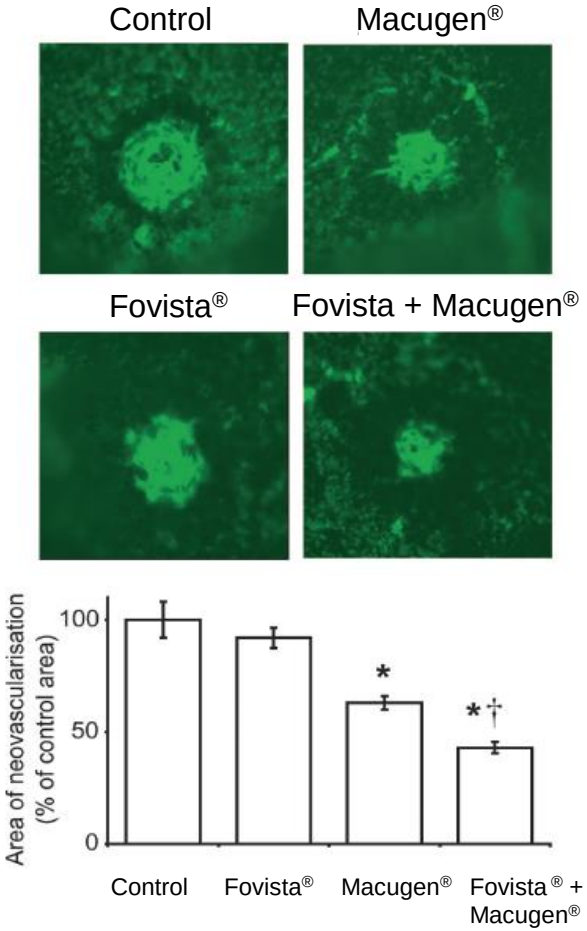


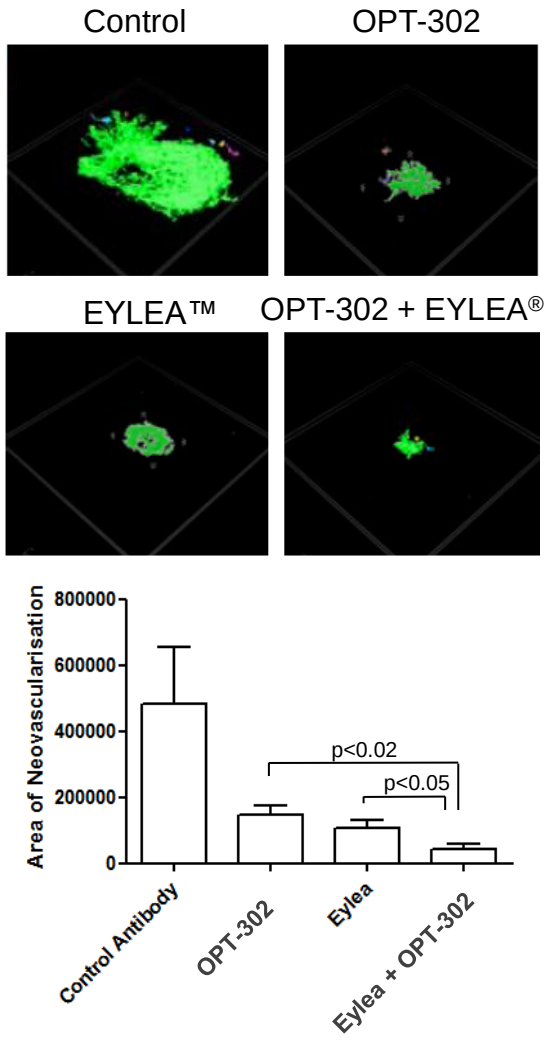
** Pairwise comparison: OPT-302 vs Eylea + OPT-302 (p<0.02)*
Eylea vs Eylea + OPT-302 (p<0.05)

OPTHEA circadian

Ophthotech and Opthea:

Distinct approaches for wet AMD combination therapy

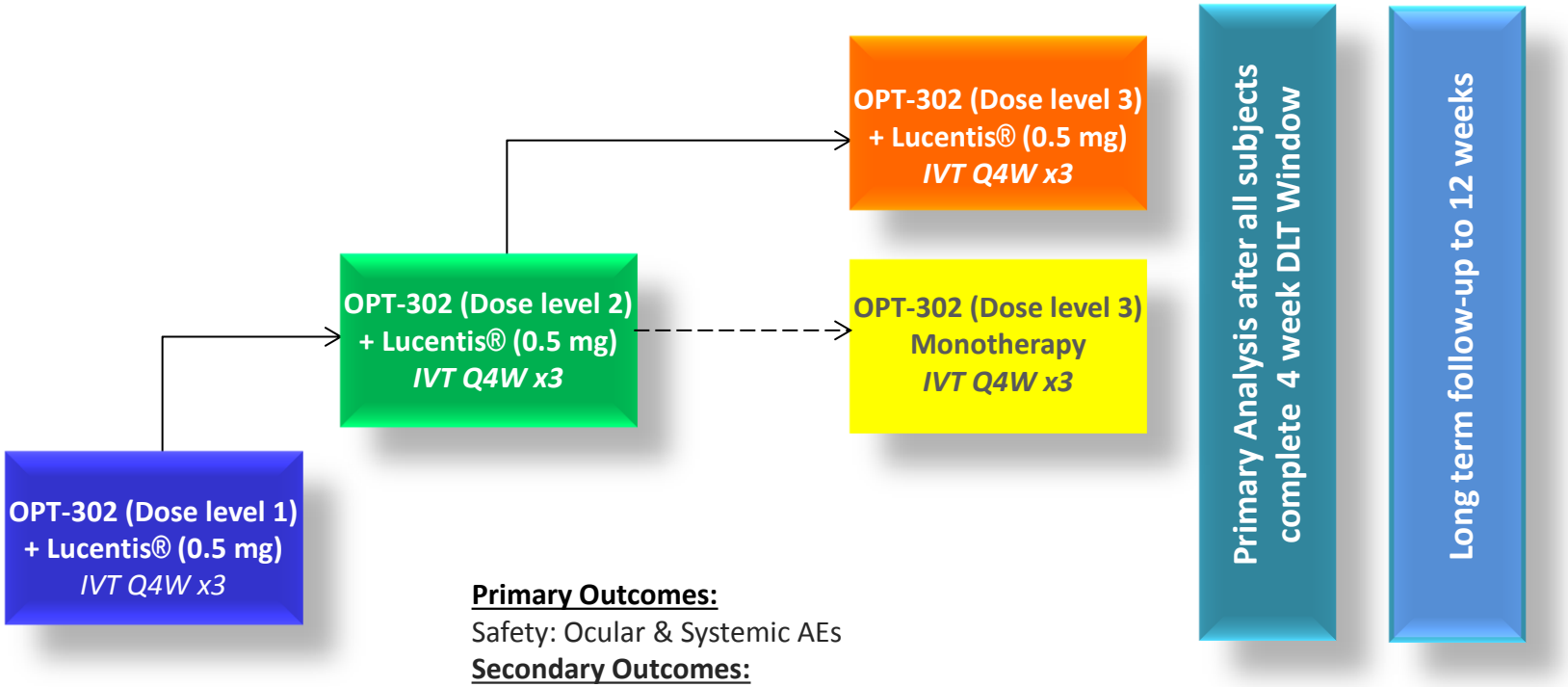




"Macugen®" – targets VEGF-A_{165} isoform
"Fovista®" – aptamer targeting PDGF-b
Jo et al., Am.J.Pathol., 168(6), 2036-2053, 2006.

OPTHEA circadian

OPT-302 Phase 1: Multiple Dose Combination & Monotherapy Study of Safety, PK & Efficacy



Primary Outcomes:

Safety: Ocular & Systemic AEs

Secondary Outcomes:

Mean change from baseline in:

- visual acuity
- central retinal thickness
- CNV area

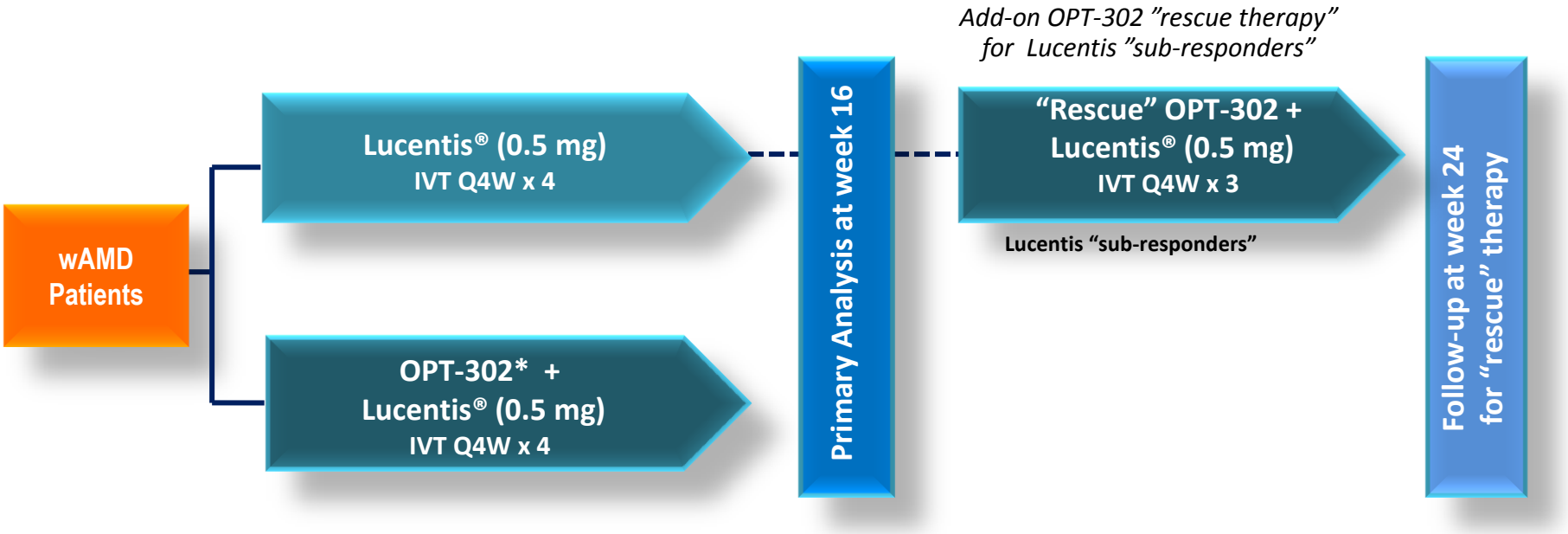
Pharmacokinetics

Anti-Drug antibody formation

Biomarkers

OPTHEA circadian

Phase 2a Efficacy Study:
OPT-302 Combination versus anti-VEGF-A Monotherapy
(including extension sub-study of OPT-302 'Rescue' therapy for a-VEGF-A "sub-responders")



Key Endpoints:

Mean change from baseline in:

- visual acuity
- central retinal thickness & fluid
- CNV area

Safety: Ocular & Systemic AEs

Pharmacokinetics

Anti-Drug antibody formation

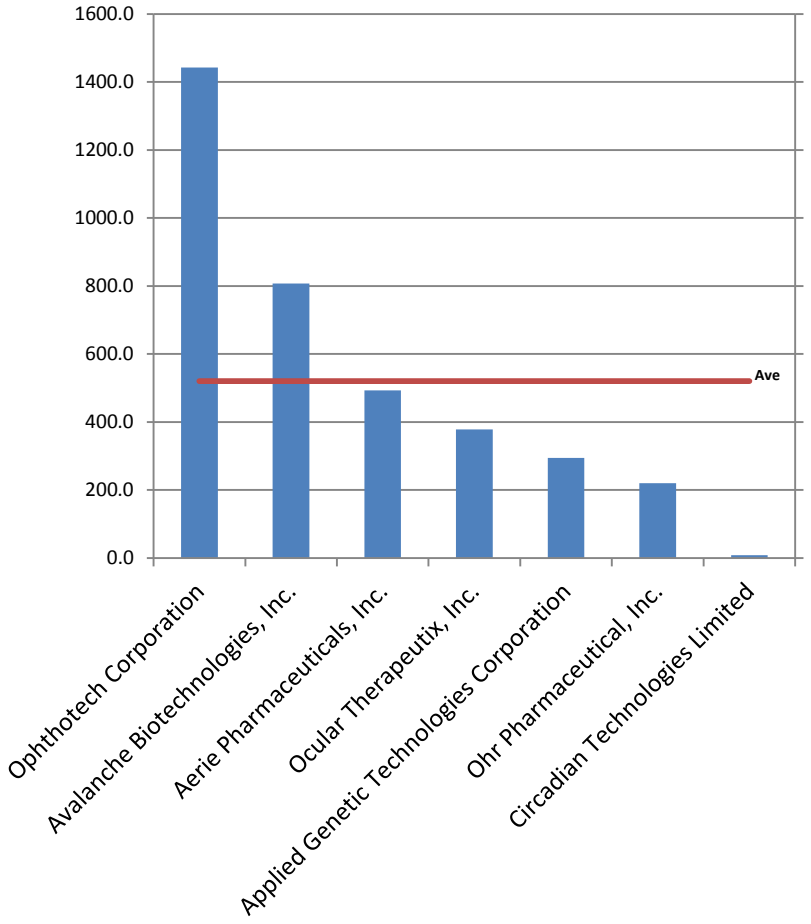
Biomarkers

** Dose level to be determined from Phase 1*

OPTHEA circadian

Listed Ophthalmology Companies in Phase 1-3

Company	Market Capitalisation (A$m)[a]	Stage of Development
Ophthotech Corporation	1442.8	Phase 3
Avalanche Biotechnologies, Inc.	807.7	Phase 1/2
Aerie Pharmaceuticals, Inc.	492.7	Phase 3
Ocular Therapeutix, Inc.	378.3	Phase 2/3
Applied Genetic Technologies Corporation	294.3	Phase 1/2
Ohr Pharmaceutical, Inc.	219.6	Phase 2
Circadian Technologies Limited	9.5	Phase 1 Start 1H15
Average	**520.6**	



a. Sept 15 2014, assumes A$1 = US$1.08

Expected News Flow

News	Estimated Date
Announce clinical advisory board	Q4'14
OPT-302 IND submission to FDA	Q2'15
OPT-302 Phase 1 clinical trial initiation in wet AMD patients	Q2'15
Primary analysis OPT-302 Phase 1 clinical trial data	Q1'16
Phase 2A clinical trial initiation	Q2'16
Primary analysis OPT-302 Phase 2A clinical trial data	Q2'17

Lead Program

OPT-302 for Wet Age-related Macular Degeneration

- The VEGF pathway is a well validated target in wet AMD
  - Annual global market for drugs targeting VEGF-A in wet AMD is in excess of $US5bn
- Impressive preclinical data provides strong positioning for OPT-302
  - Animal data as single-agent equal to existing products – Lucentis® & Eylea®
  - Data demonstrates improved efficacy in combination with approved products
  - Preclinical data with OPT-302 in combination with Eylea® demonstrates comparable activity to Fovista® (OPHT lead compound) when used in combination in the same animal model
- Extensive worldwide intellectual property platform in respect of VEGF-C, VEGF-D and VEGFR-3
- Demonstration of safety & efficacy of OPT-302 in Phase 1 and 2 trials is expected to provide a substantial uplift in valuation
- Average valuation of ophthalmology listed companies in Phase 2 development for products targeting wet AMD is >$US400mn market cap

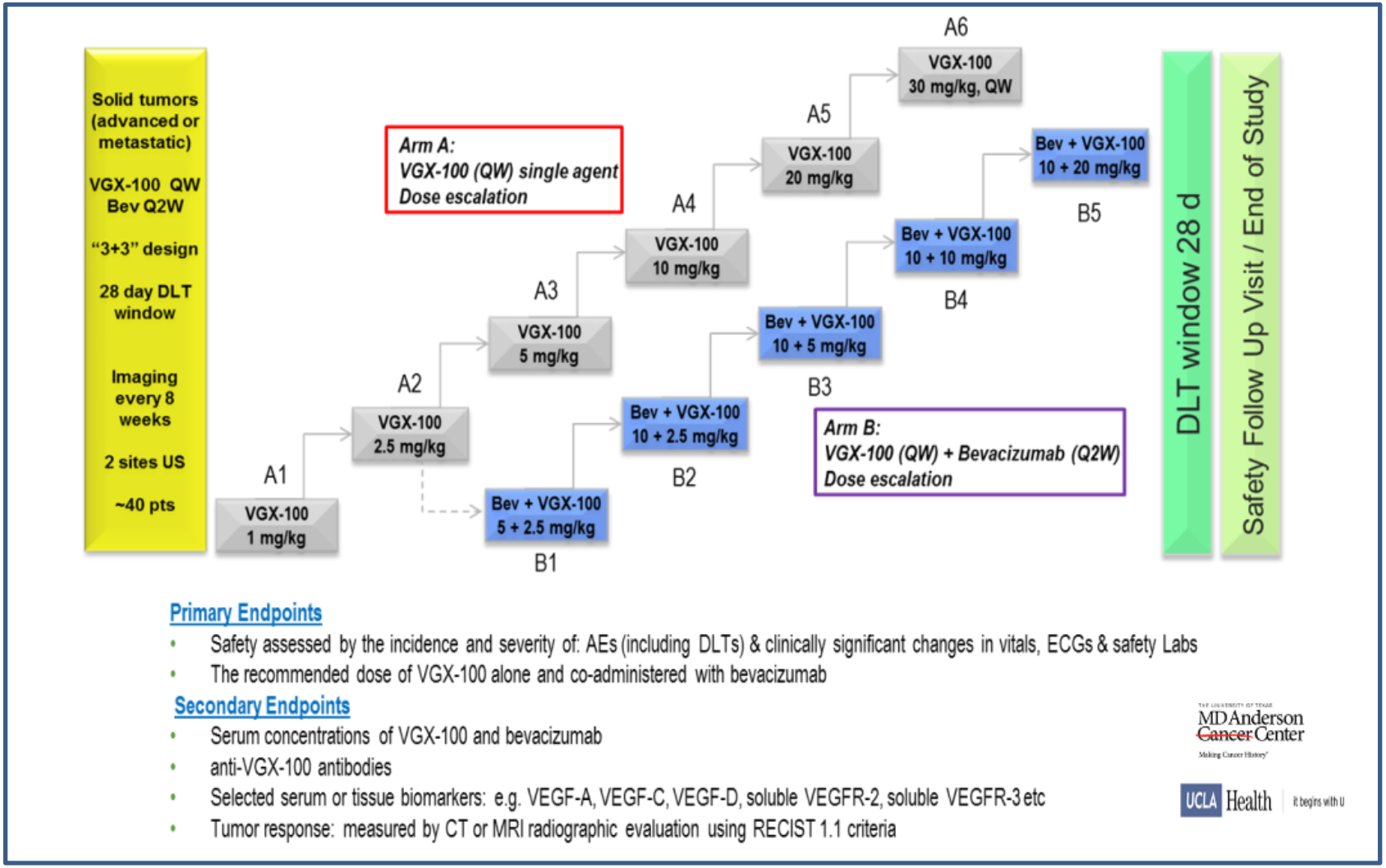
Program Update

VGX-100: A Phase 2 Ready Asset

VGX-100 is a Phase 2 ready program for oncology

- Clinical stage Phase 2 ready program
  - Positive clinical experience in 43 patients with advanced solid tumors
  - Including 24 patients when used in combination with Avastin®
  - No overlapping toxicities with anti-VEGF-A therapy
- Favourable PK (pharmacokinetic profile)
  - Supports weekly dosing
  - No anti-VGX-100 drug antibody formation
  - Doses ≥ 20 mg/kg provide adequate coverage of VEGF-C inhibition
  - Combination with Avastin® shows no drug=drug interaction
- Some patients who are refractory to standard treatments, had durable stable disease ≥ 16 weeks
- Fully human monoclonal antibody produced in good-yield, proprietary manufacturing process (Lonza)
- Comprehensive patent portfolio protecting VGX-100 at least until 2022 in US/Europe
- License/partnership opportunities

VGX-100 Oncology: Ph1a/b Trial



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

MD Anderson Cancer Center
Making Cancer History®

UCLA Health It begins with U

VGX-100 is a Phase 2 ready program for oncology

Best Response by RECIST[a]

	VGX-100 (N=19)	Bevacizumab + VGX-100 (N=24)
Evaluable Patients	17	22
Stable Disease, n (%)	6 (35)	8 (36)
Progressive Disease, n (%)	11 (65)	14 (64)

[a]In patients with measurable disease at baseline and one follow-up assessment who received at least one dose of VGX-100 (Arm A cohorts n=17; Arm B cohorts n=22).

- Five patients (13%) had durable stable disease ≥ 16 weeks
  - 2 patients with colon cancer
    - *Cohort A3: VGX-100 5 mg/kg, QW*
    - *Cohort B1: VGX-100 2.5 mg/kg, QW + Bevacizumab 5 mg/kg, Q2W*
  - 1 patient with ovarian cancer
    - *Cohort A5: VGX-100 20 mg/kg, QW*
  - 1 patient with renal cell carcinoma (RCC)
    - *Cohort B2: VGX-100 2.5 mg/kg, QW + Bevacizumab 10 mg/kg, Q2W*
  - 1 patient with cervical cancer
    - *Cohort B5: VGX-100 20 mg/kg, QW + Bevacizumab 10 mg/kg, Q2W*
- A patient with triple negative breast cancer had a 16% decrease in disease at all sites at the end of cycle 2

(Cohort B2: VGX-100 2.5 mg/kg, QW + bevacizumab 10 mg/kg, Q2W) – discontinued in cycle 3 (SAE)

Non-Core Assets

CUPGUIDE™

- Collaboration with Healthscope, Peter Mac and NICTA
- Healthscope funding ongoing clinical validation of test

VEGF-D LAM Diagnostic

- Maintain existing partnership with University of Cincinnati (UCin)
- Test offered through their Translational Trial Development and Support Laboratories, proportion of revenues to CIR
- Working with UCin towards Humanitarian Device Exemption (HDE) approval
- Funding through non-dilutive grant funding opportunities & UCin

Research Reagents

- Continue to sell VEGF-C/-D research reagents through www.vegenics.com

Syngene (52% CIR owned)

- Supported by ARC grant
- Collaborators progressing DiMiTech platform to build data package
- Management of CIR investment, plan to assess partnership opportunities

Summary

- **Leader in VEGF-C/D and VEGFR-3 targeting compounds in ophthalmology and oncology**
- Lead compound OPT-302 is a fully owned and valuable asset
  - Phase 1 clinical trial for wet age-related macular degeneration (AMD) 2Q15
  - Program expected to be funded through meaningful Phase 1 and 2A clinical milestones to Q4 2017
- Two oncology assets in clinical development
  - VGX-100 Phase 2 ready asset poised for licensing/partnership
  - Eli Lilly partnered IMC-3C5 to complete Phase 1 in solid tumours in 1H15
- Funding progresses ophthalmology program to value-adding milestones, accelerates licensing opportunities for VGX-100 and strengthens CIR balance sheet
- Clinical and business development news-flow over next 24 months
- Strong management team with experience in developing drugs targeting the VEGF pathway, wet AMD and oncology
- Extensive worldwide intellectual property platform in respect of VEGF-C/-D and VEGFR-3

Thank-you

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