OPT-302: a Phase 3-ready product to improve outcomes for patients with retinal eye diseases

Corporate Presentation, March 2021
Megan Baldwin PhD, CEO & Managing Director
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### Opthea Limited (OPT.AX, Nasdaq: OPT)

<table>
<thead>
<tr>
<th><strong>Opthea Limited</strong></th>
<th>• Public co listed on Nasdaq (OPT) and ASX (OPT.AX) developing OPT-302 for wet AMD and DME</th>
</tr>
</thead>
</table>
| **OPT-302 has a novel mechanism of action** | • OPT-302 (sVEGFR-3) is the first ‘Trap’ inhibitor of VEGF-C and VEGF-D designed specifically for the eye  
• In combination with anti-VEGF-A therapies, completely shuts-down VEGFR-2 and VEGFR-3 activity  
• Targets mechanisms of resistance and sub-optimal clinical response to existing therapies |
| **Strong & growing commercial potential** | • Current & growing market opportunity of USD12BN+ p.a. worldwide  
• OPT-302 being developed for use in combination with any of the existing anti-VEGF-A agents, biosimilars or novel therapies in development for wet AMD and DME  
• To address unmet medical need and provide superior gains in visual acuity over standard of care  
• Broad development opportunity in wet AMD, DME, RVO and other retinal pathologies |
| **Patent Coverage to 2034*** | • OPT-302 Composition of Matter patents to 2034* (granted US, EU, Australia and others)  
• *Possible Patent Term Extension, Data and Market Exclusivity in many jurisdictions |
<table>
<thead>
<tr>
<th><strong>Opthea Limited (OPT.AX, Nasdaq: OPT)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint met in Phase 2b study of OPT-302 in wet AMD</strong></td>
</tr>
<tr>
<td>Superior Vision</td>
</tr>
<tr>
<td>• OPT-302 combination therapy demonstrated <strong>superiority</strong> in visual acuity over ranibizumab (Lucentis®) at 24 weeks in a randomized, controlled, double-masked trial of 366 patients</td>
</tr>
<tr>
<td>• Secondary endpoint results also supportive of primary outcome</td>
</tr>
<tr>
<td>• Phase 2b positive data follows Phase 1/2a trial in 51 wet AMD patients</td>
</tr>
<tr>
<td><strong>Clinical Activity in Ph 2A trial of OPT-302 in persistent DME</strong></td>
</tr>
<tr>
<td>• Demonstrated activity in Phase 2a trial of OPT-302 in combination with aflibercept (Eylea®) for the treatment of persistent DME</td>
</tr>
<tr>
<td>• Completed Phase 1b dose-escalation trial in 9 persistent DME patients</td>
</tr>
<tr>
<td>• Dose-responsive improvements in visual acuity, reductions in retinal fluid &amp; swelling</td>
</tr>
<tr>
<td><strong>Well tolerated safety profile of OPT-302</strong></td>
</tr>
<tr>
<td>• Well tolerated safety profile of OPT-302 administered IVT in combination with ranibizumab &amp; aflibercept</td>
</tr>
<tr>
<td>• Extensive global clinical dosing experience with repeated IVT administration in ~400 patients across three international clinical studies in two disease indications</td>
</tr>
<tr>
<td><strong>Phase 3 Pivotal Trials in wet AMD Actively Recruiting</strong></td>
</tr>
<tr>
<td>• Two pivotal, Phase 3 clinical trials currently recruiting treatment-naïve wet patients</td>
</tr>
<tr>
<td>• US-sites open with sites opening globally over following months</td>
</tr>
<tr>
<td>• Topline data (mean change BCVA at week 52) in 2H 2023</td>
</tr>
</tbody>
</table>
Financial Position (Unaudited)

<table>
<thead>
<tr>
<th>Key Financial Details</th>
<th>Nasdaq: OPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticker Symbol</td>
<td>Nasdaq:OPT</td>
</tr>
<tr>
<td></td>
<td>ASX:OPT</td>
</tr>
<tr>
<td>Share Price (Mar 12 2021)</td>
<td>~US$9.82</td>
</tr>
<tr>
<td></td>
<td>(1 ADS: 8 ASX Ordinary shares)</td>
</tr>
<tr>
<td>Total Ordinary Shares on Issue</td>
<td>342,654,600</td>
</tr>
<tr>
<td></td>
<td>(incl. 11.6m ADS)</td>
</tr>
<tr>
<td>Market Capitalisation (Mar 12 2021)</td>
<td>~US$405m</td>
</tr>
<tr>
<td>Trading Range (last 12 months)</td>
<td>A$1.16 – 3.60</td>
</tr>
<tr>
<td>Cash Balance (Dec 31 2020)</td>
<td>~US$156m</td>
</tr>
<tr>
<td></td>
<td>(~A$202m)</td>
</tr>
<tr>
<td>Top 20 Shareholders Own</td>
<td>75%</td>
</tr>
<tr>
<td>Institutional Holders</td>
<td>87%</td>
</tr>
</tbody>
</table>

Share Price Performance (2019-2020)

![Share Price Graph](chart.png)

Analyst Coverage (Nasdaq)

- Yigal Nochomovitz
- Geoffrey Porges
- Hartaj Singh
- Robyn Karnauskas

Analyst Coverage (ASX)

- Chris Cooper
- Shane Storey
- Tanushree Jain
- Rosemary Cummins
Opthea’s Experienced Leadership Team

Management Team

- **Megan Baldwin, PhD**
  - CEO & Managing Director
  - Joined Opthea in 2008 and has been Chief Executive Officer and Managing Director since February 2014
  - **Selected Experience:** Over 20 years of experience focusing on angiogenesis and therapeutic strategies for cancer and ophthalmic indications; prior to Opthea, was employed at Genentech (now Roche)

- **Michael Tonroe**
  - CFO & Company Secretary
  - Joined Opthea in 2008 and has been Chief Executive Officer and Managing Director since February 2014
  - **Selected Experience:** Over 20 years of experience focusing on angiogenesis and therapeutic strategies for cancer and ophthalmic indications; prior to Opthea, was employed at Genentech (now Roche)

- **Richard Chadwick, PhD**
  - Head of Intellectual Property
  - Head of Intellectual Property since February 2008
  - **Selected Experience:** Qualified as both a European and Australian patent attorney, and has previously worked for FB Rice & Co., Wynne-Jones, Laine & James, Dow Corning Limited, and Unilever

- **Mike Gerometta, PhD**
  - Head of CMC Development
  - Head of Chemistry, Manufacturing and Controls Development since December 2008
  - **Selected Experience:** Has over 30 years of experience in the Australian biotech industry, working with numerous contract manufacturing organizations overseas and locally in all facets of translational CMC from concept through to Phase 2 studies

- **Clare Price**
  - Director of Clinical Development
  - Director of Clinical Development since July 2016
  - **Selected Experience:** Director of Clinical Development at Commercial Eyes Pty Ltd., and Clinical Programme Director at Starpharma Holdings Ltd.

- **Ian Leitch, PhD**
  - Director of Clinical Research
  - Director of Clinical Research since Sept 2011
  - **Selected Experience:** Senior Manager at Amgen Inc, CA and Clinical Study Director for Ophthalmology, Miravant Technologies, Santa Barbara, CA. PhD from Monash Uni.

- **Annette Leahy**
  - Director of Clinical Research
  - Director of Clinical Research since August 2017
  - **Selected Experience:** Clinical Trials Manager at Swisse Wellness Pty Ltd., and Senior Manager, Learning and Development, at Novotech (Australia) Pty Ltd.

Non-Executive Board Members

- **Jeremy Levin, DPhil, MB BChir**
  - Chairman
  - Appointed Chairman in October 2020
  - **Selected Experience:** Has extensive experience in the global biopharma industry. CEO & Chairman Ovid Therapeutics. Formerly President & CEO of Teva and Snr VP of Strategy, Alliances & Transactions at BMS.

- **Daniel Spiegelman**
  - Director
  - Appointed in September 2020 and is Chairman of the Audit & Risk Committee
  - **Selected Experience:** Former Exec Vice President & CFO, Biomarin Pharmaceutical, CFO CV Therapeutics, Board Director Myriad

- **Michael Sistenich**
  - Director
  - Appointed in November 2015, and is Chairman of the Remuneration Committee
  - **Selected Experience:** Has advised a wide range of global clients on healthcare investments over the past 20 years, and is Chairman of the Board of Enlitic

- **Lawrence Gozlan**
  - Director
  - Appointed in July 2020 & Chair of the Nomination Committee
  - **Selected Experience:** Life Sciences Investment Manager at Jagen Pty Ltd., QIC, and is a Director on several private and public company boards in AU, US

(1) Serves on the Board of Directors.
Our Goal and Strategy
To become a leader in developing & commercializing therapeutics for retinal diseases

Conduct pivotal Phase 3 clinical trials
- Advance OPT-302 through two concurrent **Phase 3 trials** for wet AMD

Optimise OPT-302 administration
- Investigate **durability** of OPT-302 treatment effect
  - OPT-302 to be administered in Phase 3 on q4w and q8w dosing schedules
  - Combination therapy may have prolonged, improved clinical efficacy over time

Develop Co-Formulation
- **Co-formulate** OPT-302 with a VEGF-A inhibitor
  - A single injection to inhibit VEGF-A/C/D
  - Advance co-formulation through IND-enabling studies and to clinic
  - Builds pipeline with VEGF-C/D ‘trap’ strategy

Expand clinical development
- Continue clinical development of OPT-302 for **DME**
- Explore potential benefit in other AMD subtypes and ocular diseases, such as PCV, RVO

Maximise commercial potential
- Broaden our geographical reach by establishing **US-based** operations in the near-term
- If approved, establish commercial operations in key territories including US and EU

PCV: Polypoidal Choroidal Vasculopathy; RVO: Retinal Vein Occlusion
Wet AMD & DME are the leading causes of vision loss in the elderly & diabetics

Increasing prevalence; large & growing market opportunity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Epidemiology (number of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet Age-Related Macular Degeneration (wAMD)</td>
<td>3.5M*</td>
</tr>
<tr>
<td>Diabetic Macular Edema (DME)</td>
<td>2M**</td>
</tr>
<tr>
<td>Macular Edema Secondary to Retinal Vein Occlusion (RVO)</td>
<td>500K*</td>
</tr>
</tbody>
</table>

Additional market opportunity:

Macular Edema Secondary to Retinal Vein Occlusion (RVO)

Characterized by retinal vein blockage, which selectively leads to edema formation and loss of visual acuity

Anti-VEGF-A Therapies are Standard of Care for wet AMD, DME and RVO

<table>
<thead>
<tr>
<th>Therapy</th>
<th>2019 Sales Revenue (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucentis</td>
<td>3.9 BN</td>
</tr>
<tr>
<td>Eylea</td>
<td>7.9 BN</td>
</tr>
</tbody>
</table>

USD 11.9 BN

~46% IVT injections administered globally are Avastin (bevacizumab), administered off-label

* US and EU; ** Worldwide
Two Major Clinical Development Areas in Wet AMD

Opthea has the potential to improve EFFICACY and DURABILITY of treatment.

- **Next Generation anti-VEGF-A therapies**
  - **DURABILITY**
    - To reduce # injections
    - Not intended to improve patient responses

- **New Therapies Targeting Novel Pathways**
  - **EFFICACY**
    - To improve patient outcomes
    - Improve VISION

“Combination Therapy”
Existing Therapies Primarily Target VEGF-A

OPT-302 has potential to improve clinical Efficacy & Durability by targeting VEGF-C/D

OPT-302 inhibits VEGF-C/D

- Ranibizumab (Lucentis®)
- Brolucizumab (Beovu®)
- Bevacizumab® (Avastin®)
- Aflibercept (Eylea®)
- VEGF-A
- VEGF-B
- PIGF
- VEGF-C
- VEGF-D
- OPT-302

OPT-302: Rationale

- Long-term therapy with selective VEGF-A inhibitors is associated with sub-optimal responses
  - Sub-optimal improvements in visual acuity
  - Persistent retinal fluid
- Resistance to VEGF-A monotherapy may be related to other VEGF family members
- VEGF-C/D signal for angiogenesis and vascular permeability independently of VEGF-A; and
- VEGF-C/D are elevated when VEGF-A is inhibited
- OPT-302 combination therapy achieves broad suppression of the VEGF/VEGFR pathway
- OPT-302 targets incomplete response to VEGF-A inhibition & validated pathway involved in wet AMD and DME progression

Used in combination with a VEGF-A inhibitor, completely blocks VEGF-2 and VEGF-3 signalling, broadly suppressing VEGF/VEGFR pathway

* Bevacizumab is used ‘off-label’ for the treatment of nAMD
A Currently Unmet Medical Need for wet AMD and DME
Clinical data suggest VEGF-C/D may mediate resistance & sub-optimal response to anti-VEGF-A therapy

**Wet AMD Patients**

<table>
<thead>
<tr>
<th>Aqueous Humor VEGF-C (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Bevacizumab</td>
</tr>
<tr>
<td>Bevacizumab</td>
</tr>
</tbody>
</table>

**Despite receiving a VEGF-A inhibitor (ranibizumab, aflibercept or bevacizumab)**:

- **wet AMD**
  - >45%: Do not achieve significant vision gains
  - 2/3: Will continue to have fluid at the back of the eye
  - 25%: Will have further vision loss at 12 months

- **DME**
  - 2/3: Do not achieve significant vision gains
  - 25%: Continue to have macula thickening/swelling

**Opportunity: New Products that have Potential to Improve Efficacy and Durability**

**Opthea’s strategy is to develop OPT-302 as a combination therapy to be administered with any of the approved a-VEGF-A therapies or new VEGF-A inhibitors in development**

VEGF-C/D activate VEGFR-2 and -3 independently of VEGF-A, and are upregulated when VEGF-A is inhibited.

* Based on randomised, controlled clinical trial data; # Fail to achieve ≥ 2 lines improvement in BCVA; ^ SD-OCT CST ≥ 300 µM or Time-Domain OCT CST ≥ 250 µM
OPT-302: A ‘trap’ inhibitor of VEGF-C and VEGF-D

OPT-302 combination therapy may improve treatment EFFICACY and DURABILITY

OPT-302: A soluble form of VEGFR-3

- A ‘trap’ comprising the extracellular domains 1-3 of VEGFR-3 and the Fc fragment of human IgG1
- Potent inhibitor of VEGF-C (~5 pM) and VEGF-D (~0.5 nM)
- In development for use in combination with inhibitors of VEGF-A as a:
  - Sequential injection – Provides treatment flexibility
  - Co-formulation – Single injection VEGF-A & VEGF-C/D inhibition
- To demonstrate superior gains in visual acuity in patients
- To investigate efficacy and durability of OPT-302 administered on an every four- and every eight-week dosing cycle (q4w, q8w)
- To provide physicians with a new treatment option targeting a novel mechanism that is complementary to standard of care treatments targeting VEGF-A
- Currently a scarcity of novel approaches that may address the sub-optimal clinical responses that many patients experience on anti-VEGF-A therapies

Addressing EFFICACY & DURABILITY

- Potential for prolonged clinical efficacy over time
- OPT-302 has characteristics to ‘match’ extended dosing regimens of approved anti-VEGF-A therapies and emerging agents:
  - OPT-302 is structurally similar to aflibercept (OPT-302 is larger VEGF-receptor ‘trap’ at ~140kDa)
  - OPT-302 has comparable ocular biodistribution to aflibercept (rabbit study)
  - Similar PK profile and half-life of OPT-302 in the vitreous following IVT administration to rabbits, with low systemic exposure
## Pipeline

### Wet Age-Related Macular Degeneration (Wet AMD)

<table>
<thead>
<tr>
<th>Product</th>
<th>Clinical Trials &amp; Combination Agent(s)</th>
<th>Research/Preclinical</th>
<th>Phase 1</th>
<th>Phase 2a</th>
<th>Phase 2b</th>
<th>Phase 3</th>
<th>Next Anticipated Milestone</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPT-302</td>
<td>Completed Phase 2b: Ranibizumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1H 2021: Initiation of two concurrent Phase 3 trials</td>
<td>OPTHEA (Worldwide)</td>
</tr>
<tr>
<td></td>
<td>Two planned Phase 3 trials: Ranibizumab (ShORe), Aflibercept (COAST)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2023: Phase 3 top-line data</td>
<td></td>
</tr>
</tbody>
</table>

### Diabetic Macular Edema (DME)

<table>
<thead>
<tr>
<th>Product</th>
<th>Clinical Trials &amp; Combination Agent(s)</th>
<th>Research/Preclinical</th>
<th>Phase 1</th>
<th>Phase 2a</th>
<th>Phase 2b</th>
<th>Phase 3</th>
<th>Next Anticipated Milestone</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPT-302</td>
<td>Phase 1b/2a: Aflibercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Company may choose to initiate study in DME</td>
<td>OPTHEA (Worldwide)</td>
</tr>
</tbody>
</table>

### Co-Formulation (OPT-302 + VEGF-A Inhibitor) (Wet AMD)

<table>
<thead>
<tr>
<th>Co-Formulated OPT-302 + VEGF-A Inhibitor</th>
<th>Clinical Trials &amp; Combination Agent(s)</th>
<th>Research/Preclinical</th>
<th>Phase 1</th>
<th>Phase 2a</th>
<th>Phase 2b</th>
<th>Phase 3</th>
<th>Next Anticipated Milestone</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target: VEGF-C/D &amp; VEGF-A</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>2H 2021: File IND (FDA)</td>
<td>OPTHEA (Worldwide)</td>
</tr>
</tbody>
</table>
Phase 3 Pivotal Trials in Wet AMD

Initiated March 2021
Topline Data 2H 2023

Two concurrent, randomized, controlled, 3-arm Phase 3 studies investigating OPT-302 administered every four-weeks and every-eight weeks in combination with standard of care anti-VEGF-A therapy:

ShORe: Study of OPT-302 in combination with Ranibizumab (Study OPT-302-1004)
COAST: Combination OPT-302 with Aflibercept STudy (Study OPT-302-1005)
**OPT-302 Phase 3 Pivotal Program**

**Trial initiations early 2021**

### ShORe

**Study of OPT-302 in combination with Ranibizumab**

- **Sample size:** 330 patients per arm, 990 per study
- **Primary Objective:** Mean change from Baseline in BCVA at Wk 52
- **Design:** Multi-centre, double-masked, randomised (1:1:1), sham control
- **Regulatory quality:** 90% power, 5% type I error rate

* Sham administered at visits when OPT-302 is not administered

### COAST

**Combination OPT-302 with Aflibercept Study**

- **Sample size:** 330 patients per arm, 990 per study
- **Primary Objective:** Mean change from Baseline in BCVA at Wk 52
Opthea’s Clinical Data:

Phase 1/2a trial in treatment naïve and prior treated wet AMD patients (n=51)

Phase 2b randomized, controlled, double-masked & statistically powered wet AMD trial (n=366)

Phase 1b/2a trial in prior-treated DME patients
Phase 1/2a study: OPT-302 well-tolerated and active in wet AMD (Summary)

Visual acuity benefit observed as monotherapy & in combination with ranibizumab

Visual Acuity Gains (Baseline to Wk 12) following Monotherapy OPT-302 (q4w x3)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Visual Acuity (Mean Change from Baseline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>-6.4 (-1.6)</td>
</tr>
<tr>
<td>Week 8</td>
<td>0.6 (+0.2)</td>
</tr>
<tr>
<td>Week 12</td>
<td>5.5 (+1.0)</td>
</tr>
</tbody>
</table>

- **Treatment-Naive**
- **Prior Treated**

OPT-302 Phase 1/2a Key Take-Aways

- OPT-302 met the primary safety objective of its Phase 1/2a study (well tolerated)
- Study (n=51) recruited treatment naïve (49%) and heavily pre-treated patients (51%), and a high proportion of patients with occult (73%) wet AMD lesions:
  - **Naïve Patients**:
    - Mean gain in visual acuity at week 12 from baseline was +10.8 letters vs. +5.9 letters for Lucentis alone in the MARINA trial and +6.1 letters for each of Avastin and Lucentis alone in the CATT study
  - **Prior Treated Patients**:
    - Patients had received an average of 17 prior injections, equating to prior treatment over an average ~1.3 years
    - Mean gain in visual acuity at week 12 from baseline was +4.9 letters
    - Mean reductions in CST and SRF at week 12 of 54 mM and 62 mM (51%), respectively, from baseline
  - **Monotherapy Patients**:
    - Evidence of clinical activity and visual acuity gains without background standard of care
    - Mean gain in visual acuity at week 12 from baseline of +5.6 letters for patients who did not require “rescue” therapy (7/13, or 54% of patients)

- A consistency of responses in patients with different treatment histories & across various secondary outcome measures (VA, OCT)
- Phase 1/2a trial results supportive of progressing to larger, randomised, controlled Phase 2b study

Phase 2b

A multicenter, randomized, double-masked, sham controlled study of intravitreal OPT-302 in combination with ranibizumab, in participants with neovascular (wet) AMD

Conducted at 109 sites across 10 countries: US, EU, Israel

OPT-302-1002; NCT ClinicalTrials.gov Identifier: NCT03345082
Study Overview

### Screening
- **Key Inclusion Criteria**
  - Active CNV ≥50% lesion, classic / minimally classic / occult
  - BCVA ≥ 25 and ≤ 60 letters

### Treatment naïve patients with neovascular AMD

### Key Exclusion Criteria
- Subfoveal fibrosis or >25% of total lesion
- Haemorrhage >50% total lesion
- Other clinically significant ocular disease

### Randomised (n=366)

### Allocation

**ITT Population**
- **sham + 0.5 mg ranibizumab IVT**
  - Q4W x 6
  - n=121
- **OPT-302 0.5 mg + 0.5 mg ranibizumab IVT**
  - Q4W x 6
  - n=122
- **OPT-302 2.0 mg + 0.5 mg ranibizumab IVT**
  - Q4W x 6
  - n=123

### Follow-up
- **Completed Study**
  - n=116 (95.9%)
  - n=112 (91.8%)
  - n=120 (97.6%)

### Analysis

**mITT Population**
- **Analysed**
  - n=119
  - n=122
  - n=121

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CNV – choroidal neovascularisation; IVT – intravitreal; Q4W – once every 4 weeks

ITT – Intent to Treat Population, all participants who were randomised into the study irrespective of whether study medication was administered or not

Safety Population - all participants in the ITT but excluding those who did not receive at least one dose of study medication

mITT – Modified ITT Population, all participants in the Safety Population but excludes any participant without a Baseline VA score and/or any participant who did not return for at least one post-baseline visit.
Study Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Demographic / Baseline Disease Characteristic</th>
<th>Sham + ranibizumab N=121</th>
<th>0.5 mg OPT-302 + ranibizumab N=122</th>
<th>2.0 mg OPT-302 + ranibizumab N=123</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age – years ± SD</td>
<td>76.1 ± 9.48</td>
<td>78.8 ± 8.16</td>
<td>77.8 ± 8.82</td>
</tr>
<tr>
<td>Sex – n (%)</td>
<td>Male</td>
<td>48 (39.7%)</td>
<td>49 (40.2%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>73 (60.3%)</td>
<td>73 (59.8%)</td>
</tr>
<tr>
<td>Caucasian Race – n (%)</td>
<td>117 (99.2%)</td>
<td>119 (99.2%)</td>
<td>117 (97.5%)</td>
</tr>
<tr>
<td>Mean Visual Acuity (BCVA) – letters ± SD</td>
<td>50.7 ± 10.21</td>
<td>51.1 ± 8.96</td>
<td>49.5 ± 10.26</td>
</tr>
<tr>
<td>Mean Total Lesion Area - mm² ± SD</td>
<td>6.08 ± 3.21</td>
<td>6.48 ± 3.30</td>
<td>6.62 ± 3.39</td>
</tr>
<tr>
<td>Lesion Type</td>
<td>Predominantly classic – n (%)</td>
<td>15 (12.4%)</td>
<td>15 (12.3%)</td>
</tr>
<tr>
<td></td>
<td>Minimally classic – n (%)</td>
<td>53 (43.8%)</td>
<td>51 (41.8%)</td>
</tr>
<tr>
<td></td>
<td>Occult - n (%)</td>
<td>53 (43.8%)</td>
<td>56 (45.9%)</td>
</tr>
<tr>
<td></td>
<td>PCV detected¹ – n (%)</td>
<td>20 (16.5%)</td>
<td>24 (19.7%)</td>
</tr>
<tr>
<td></td>
<td>RAP detected² – n (%)</td>
<td>15 (12.7%)</td>
<td>22 (18.5%)</td>
</tr>
<tr>
<td>Mean central subfield thickness (CST) - mm ±SD</td>
<td>412.10 ± 110.62</td>
<td>425.18 ± 120.45</td>
<td>414.12 ± 123.25</td>
</tr>
<tr>
<td>Sub-retinal fluid (SRF) present – % participants</td>
<td>89.3%</td>
<td>84.4%</td>
<td>87.8%</td>
</tr>
<tr>
<td>Intra-retinal cysts present – % participants</td>
<td>57.9%</td>
<td>63.9%</td>
<td>56.1%</td>
</tr>
</tbody>
</table>

Intent-to-Treat (ITT) population; SD: standard deviation; BCVA: Best Corrected Visual Acuity

¹ PCV - polypoidal choroidal vasculopathy, detected by SD-OCT, FA and fundus photography
² RAP - retinal angiomatous proliferation, detected by SD-OCT, FA and fundus photography
OPT-302 (2.0 mg) Combination Therapy Demonstrated Superiority in Visual Acuity over Ranibizumab

Primary Endpoint Achieved: Mean Change in Best Corrected Visual Acuity Baseline to Week 24

\[ \Delta = +3.4 \ (p=0.0107) \]

Mean change in BCVA (SEM) (letters)

Sham + 0.5 mg ranibizumab (n=119)
0.5 mg OPT-302 + 0.5 mg ranibizumab (n=122)
2.0 mg OPT-302 + 0.5 mg ranibizumab (n=121)

mITT; BCVA – best corrected visual acuity
Left: Difference in Least Square Means, using Model for Repeated Measures (MRM) analysis. Right: Graph represents “as observed” data and SEM.
Reduced Retinal Thickness & Better ‘Retinal Drying’

With OPT-302 Combination Therapy

Mean Change in CST – Baseline to Week 24

% Participants with SRF present

% Participants with IR Cysts present

Mean change in CST (SEM)

Sham + 0.5 mg ranibizumab (n=116)
2.0 mg OPT-302 + 0.5 mg ranibizumab (n=119)

Mean Change in CST – Baseline to Week 24

% Participants with SRF present

% Participants with IR Cysts present

Modified Intent-to-Treat (mITT) population; as observed; CST – central subfield thickness; SRF – sub-retinal fluid; IR – intra-retinal
Greater Reduction in Total Lesion and CNV Area
With OPT-302 Combination Therapy

Modified Intent-to-Treat (mITT) population; as observed; CNV – choroidal neovascularisation; Difference in Least Square Means
Neovascular (wet) AMD Lesion Types
Differ in vessel location, leakiness and responsiveness to VEGF-A inhibitors

- **OCCULT**
  - 100% beneath RPE
  - Least responsive to VEGF-A inhibition

- **MINIMALY CLASSIC**
  - <50% vessels above RPE
  - Moderately responsive to VEGF-A inhibition

- **PREDOMINANTLY CLASSIC**
  - ≥50% vessels above RPE
  - Highly responsive to VEGF-A inhibition
Mean Change in Visual Acuity Over Time by Lesion Type

Patients with minimally classic & occult lesions have best response; small number predominantly classic patients

mITT; as observed. BCVA: Best-Corrected Visual Acuity
Retinal Angiomatous Proliferation (RAP) Lesions
Have a distinct biology and vessel proliferation occurs within the retina (not the choroid)

STAGE 1
Intraretinal neovascularization

STAGE 2
Subretinal neovascularization with retinal-retinal anastomosis

STAGE 2 with PED
Subretinal neovascularization with a pigment epithelial detachment

STAGE 3
Choroidal neovascularization with a vascularized pigment epithelial detachment and retinal-retinal anastomosis
Improved Visual Acuity in OPT-302 + ranibizumab treated patients

Mean change in Visual Acuity to Week 24 in participants without RAP at baseline (>86% study participants)

mITT; RAP – retinal angiomatous proliferation;
Least square means (LSM) determined using Model for Repeated Measures (MRM) analysis (adjusted for baseline vision and lesion type as used in the randomisation as covariates).
Greater visual acuity gain in patients with lesions consisting of a majority of occult vessels (RAP Absent)

mITT, as observed, $\Delta$ based on least square means determined using Model for Repeated Measures (MRM) analysis (adjusted for baseline vision and lesion type (randomisation) as covariates).
Improved Visual Acuity in patients with Min.Classic/Occult lesions (RAP Absent)
Represents primary analysis patient population in planned Phase 3 trials

mitT; Least square means (LSM) determined using Model for Repeated Measures (MRM) analysis (adjusted for baseline vision and lesion type as used in the randomisation as covariates).
<table>
<thead>
<tr>
<th>N Participants (%)</th>
<th>Sham + ranibizumab N=121</th>
<th>0.5 mg OPT-302 + ranibizumab N=120</th>
<th>2.0 mg OPT-302 + ranibizumab N=124</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment emergent AEs (TEAEs)</td>
<td>84 (69.4%)</td>
<td>87 (72.5%)</td>
<td>93 (75.0%)</td>
</tr>
<tr>
<td>Ocular AEs - Study Eye – related to study product(s)</td>
<td>17 (14.0%)</td>
<td>17 (14.2%)</td>
<td>19 (15.3%)</td>
</tr>
<tr>
<td>Ocular AEs - Study Eye – Severe</td>
<td>1 (0.8%)</td>
<td>2 (1.7%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>10 (8.3%)</td>
<td>16 (13.3%)</td>
<td>7 (5.6%)</td>
</tr>
<tr>
<td>Ocular SAEs in Study Eye</td>
<td>0 (0.0%)</td>
<td>2 (1.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Intraocular inflammation</td>
<td>2^5,6 (1.7%)</td>
<td>2^5 (1.7%)</td>
<td>1^5 (0.8%)</td>
</tr>
<tr>
<td>Participants with AEs leading to study IP discontinuation only</td>
<td>2 (1.7%)</td>
<td>3 (2.5%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Participants with AEs leading to study discontinuation</td>
<td>1^6 (0.8%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Any APTC event</td>
<td>0 (0.0%)</td>
<td>1^8 (0.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Deaths</td>
<td>2^9 (1.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Safety population analysed according to medication received

1 Assessed by investigator to be “possibly related”, “probably related” or “definitely related” to administration of study drug(s)
2 Assessed by Investigator to be National Institutes of Health (NIH) Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or above, or, if CTCAE grade is unavailable, an AE assessed as “causing an inability to perform normal daily activities”
3 SAE of endophthalmitis, with AEs of hypopyon and anterior chamber cell (n=1), SAE of vitritis (n=1)
4 AEs considered to be indicative of intraocular inflammation, defined prior to database lock as: Endophthalmitis, iritis, vitritis, iridocyclitis, uveitis, hypopyon, viral iritis, or anterior chamber inflammation
5 Transient anterior chamber cell (trace 1-4 cells)
6 Not reported as a TEAE
7 Squamous cell carcinoma of the lung diagnosed shortly after Baseline visit
8 Non-fatal myocardial infarction
9 Pneumonia (n=1), infective endocarditis (n=1)
Conclusions – OPT-302 Phase 2b wet AMD Trial

• Phase 2b trial met primary endpoint
  • OPT-302 (2.0 mg) combination therapy demonstrated superiority in visual acuity over ranibizumab + sham
  • Vision gain of +3.4 letters
  • Statistically significant (p=0.0107)
  • High ranibizumab control arm

• Secondary outcomes were supportive of the primary endpoint:
  • Vision
    • More patients gained ≥ 15, ≥10 and ≥5 letters of vision
    • Fewer patients lost ≥ 15, ≥10 and ≥5 letters of vision
  • Retinal anatomical improvements
    • Reductions in CST, subretinal and intraretinal fluid
    • Greater decreases in Total Lesion Area and CNV Area

• Minimally Classic / Occult Lesions:
  • **+5.7 letter gain** in visual acuity in minimally classic/occult lesions treated with OPT-302 combination therapy compared to standard of care
  • Represents primary analysis patient population in planned Phase 3 trials
  • Greater activity of OPT-302 in lesion-types considered more difficult to treat with anti-VEGF-A therapy & highest unmet need

• Favorable tolerability profile similar to ranibizumab alone
Phase 3 Pivotal Trials

**Wet AMD**

Two concurrent, randomized, controlled, 3-arm Phase 3 studies investigating OPT-302 administered every four-weeks and every-eight weeks in combination with standard of care anti-VEGF-A therapy:

**ShORe:** Study of OPT-302 in combination with Ranibizumab (Study OPT-302-1004)

**COAST:** Combination OPT-302 with Aflibercept Study (Study OPT-302-1005)
**OPT-302 Phase 3 Pivotal Program**

Trial initiations early 2021

**ShORe**  
Study of OPT-302 in combination with Ranibizumab

- **Sample size:** 330 patients per arm, 990 per study
- **Primary Objective:** Mean change from Baseline in BCVA at Wk 52

**Design:** Multi-centre, double-masked, randomised (1:1:1), sham control

**Regulatory quality:** 90% power, 5% type I error rate

* Sham administered at visits when OPT-302 is not administered

**COAST**  
Combination OPT-302 with Aflibercept Study
Opthea’s Phase 3 design is Optimised for Success based on Ph2b outcomes

- **We know the patients which respond best:**
  - Analyse these patients first (min.classic & occult)
  - Maximises opportunity to demonstrate most compelling vision benefit
  - In Phase 2b, +5.7 letters superior benefit of OPT-302 combination therapy compared to Lucentis alone

- **Design Phase 3 trials to maximise commercial opportunity:**
  - Recruit ‘all-comer’ wet AMD patient population, but analyse total population following analysis in min.classic & occult patients first
  - ShORe and COAST investigate OPT-302 in combination with two leading standard of care treatments respectively
  - Positions OPT-302 for use in combination with any VEGF-A inhibitor

- **Designed for ‘multiple-shots’ on goal:**
  - Analysis in min.classic/occult patients, and in total patient population
  - Analysis of efficacy on q4w and q8w dosing regimens provides insight into OPT-302 durability

- **End of Phase 2 and Scientific Advice meetings completed with U.S. FDA and European Medicines Agency (EMA)**
  - Company intends to submit BLA and MAA with FDA and EMA following completion of the primary efficacy phase
Phase 1b/2a Trial of OPT-302 Combination Therapy for Persistent DME

Phase 1b/2a study of OPT-302 in combination with aflibercept for persistent central-involved diabetic macular edema
OPT-302 DME Trial Design
Previously anti-VEGF-A-treated patients with persistent DME, a difficult-to-treat population

Key Inclusion Criteria

- Age ≥ 18 years; centre-involving DME
- CST ≥ 320 µm*
- BCVA 73 – 24 ETDRS letters (20/40 – 20/320 Snellen)
- Prior exposure to anti-VEGF-A therapy
  - ≥ 3 intravitreal injections in last 5 months prior to study day 1
  - Last injection ≤ 42 days prior to study day 1
  - Prior off-label bevacizumab only allowed if switched to ≥ 1 injection of aflibercept or ranibizumab prior to study
- HbA1c ≥ 12%
- Uncontrolled hypertension ≥ 180 mmHg systolic or ≥ 110 mmHg diastolic
- Eyes needing PRP within 3 months of screening
- Concurrent / prior use of intravitreal injections of steroids within 4 months of study start
- Concurrent / prior dexamethasone or fluocinolone implant in study eye

Key Exclusion Criteria

- Hba1c ≥ 12%
- Uncontrolled hypertension ≥ 180 mmHg systolic or ≥ 110 mmHg diastolic
- Eyes needing PRP within 3 months of screening
- Concurrent / prior use of intravitreal injections of steroids within 4 months of study start
- Concurrent / prior dexamethasone or fluocinolone implant in study eye

OPT-302-1003 Phase 1b/2a clinical trial (NCT03397264)
*CST as measured by Spectralis (Heidelberg) at screening, ≥ 305 µm for Cirrus. # 144 patients randomized in the trial, 115 conformed sufficiently with the trial protocol and were included in clinical efficacy analyses.
DRT, Dose Limiting Toxicity; Q4W, once every 4 weeks; VEGF, vascular endothelial growth factor.
Phase 1b/2a Clinical Analyses of OPT-302 Combination Therapy
All patients enrolled had persistent center-involved DME despite prior anti-VEGF-A treatment

✓ Favorable tolerability profile in combination with aflibercept
✓ Dose-responsive improvements in visual acuity, reductions in retinal fluid & swelling
✓ Phase 2a primary efficacy endpoint achieved
✓ Totality of secondary functional and anatomical responses indicate OPT-302 activity
✓ Greatest visual acuity gains in patients with prior-treatment history of aflibercept
Phase 1b Dose Escalation of OPT-302 Combination Therapy

Summary of results

Previously anti-VEGF-A treated patients with center-involved DME (N=9)

- OPT-302 (0.3 mg) + aflibercept (2 mg) IVT Q4W x 3
- OPT-302 (1 mg) + aflibercept (2 mg) IVT Q4W x 3
- OPT-302 (2 mg) + aflibercept (2 mg) IVT Q4W x 3

Safety / Tolerability:
- IVT OPT-302 up to 2 mg in combination with aflibercept (2 mg) was well tolerated
- No dose limiting toxicities
- Maximum Tolerated Dose not reached
- No study drug related adverse events

- OPT-302 + Aflibercept showed a dose-response for BCVA gains to Week 12 with a corresponding decrease in CST

Safety & Tolerability:
- IVT OPT-302 up to 2 mg in combination with aflibercept (2 mg) was well tolerated
- No dose limiting toxicities
- Maximum Tolerated Dose not reached
- No study drug related adverse events

![Graph showing mean change in BCVA and CST over weeks]

- Mean change in BCVA (SEM) for OPT-302 and aflibercept combination
- Mean change in CST (SEM) for OPT-302 and aflibercept combination

IVT – intravitreal; Q4W – once very 4 weeks
Approximately one third of patients received regular prior aflibercept therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2.0 mg aflibercept + Sham (N=40)</th>
<th>2.0 mg aflibercept + 2.0 mg OPT-302 (N=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Duration of Diabetic Macular Edema – years (±SD)</td>
<td>1.6 (1.70)</td>
<td>1.3 (1.30)</td>
</tr>
<tr>
<td>Mean Number of Prior IVT Anti-VEGF-A Injections for CI-DME (±SD)</td>
<td>8.4 (4.56)</td>
<td>8.0 (4.35)</td>
</tr>
<tr>
<td>Mean Duration of Prior IVT Anti-VEGF-A injections – months (±SD)</td>
<td>12.4 (6.43)</td>
<td>10.7 (5.95)</td>
</tr>
<tr>
<td>Mean time from Prior Treatment to Day 1 – days (±SD)</td>
<td>38.4 (3.59)</td>
<td>38.8 (3.87)</td>
</tr>
</tbody>
</table>

Prior Anti-VEGF-A Therapies n (%)

<table>
<thead>
<tr>
<th></th>
<th>2.0 mg aflibercept + Sham (N=40)</th>
<th>2.0 mg aflibercept + 2.0 mg OPT-302 (N=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 injections</td>
<td>4 (10.0%)</td>
<td>6 (8.0%)</td>
</tr>
<tr>
<td>4-6 injections</td>
<td>13 (32.5%)</td>
<td>33 (44.0%)</td>
</tr>
<tr>
<td>7-12 injections</td>
<td>15 (37.5%)</td>
<td>24 (32.0%)</td>
</tr>
<tr>
<td>13-24 injections</td>
<td>8 (20.0%)</td>
<td>12 (16.0%)</td>
</tr>
</tbody>
</table>

Prior Anti-VEGF-A Treatment n (%)

<table>
<thead>
<tr>
<th></th>
<th>2.0 mg aflibercept + Sham (N=40)</th>
<th>2.0 mg aflibercept + 2.0 mg OPT-302 (N=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflibercept a</td>
<td>13 (32.5%)</td>
<td>22 (29.3%)</td>
</tr>
<tr>
<td>Ranibizumab b</td>
<td>4 (10.0%)</td>
<td>9 (12.0%)</td>
</tr>
<tr>
<td>Bevacizumab c</td>
<td>18 (45.0%)</td>
<td>32 (42.7%)</td>
</tr>
<tr>
<td>Multiple switching of anti-VEGF-A therapy (aflibercept, ranibizumab, bevacizumab) d</td>
<td>5 (12.5%)</td>
<td>12 (16.0%)</td>
</tr>
</tbody>
</table>

Per Protocol population (n=115), must have received all 3 intravitreal study treatments and evaluable at Baseline through Week 12 and sufficiently compliant with the protocol.

a Includes patients receiving only all Afiblercept or last 3 injections of Afiblercept prior to study entry

b Includes patients receiving only all Ranibizumab or last 3 injections of Ranibizumab prior to study entry

c Includes patients receiving only all Bevacizumab. For last injection prior to study entry patients must be switched to 1 injection of either Afiblercept or Ranibizumab

d Includes patients receiving multiple switching of anti-VEGF-A therapy. For last injection prior to study entry patients must be switched to 1 injection of either Afiblercept or Ranibizumab
Visual Acuity Gain following OPT-302 combination therapy
Exploratory Subgroup Analysis in patient population with a prior treatment history of aflibercept

Mean Change in BCVA Baseline to Week 12

Per Protocol population prior aflibercept subgroup (n=35), must have received all 3 intravitreal study treatments and evaluable at Baseline through Week 12 and sufficiently compliant with the protocol. Error bars (± SEM)
Gains in Visual Function, Reduced Vision Loss with OPT-302

Exploratory Subgroup Analysis in patient population with a prior treatment history of aflibercept

- **≥10 Letter Gain At Week 12**
- **≥15 Letter Gain At Week 12**
- **≥1 Letter Loss At Week 12**

Per Protocol population prior aflibercept subgroup (n=35), must have received all 3 intravitreal study treatments and evaluable at Baseline through Week 12 and sufficiently compliant with the protocol.
Reduction of Retinal Thickness
Exploratory Subgroup Analysis in patient population with a prior treatment history of aflibercept

Mean Change in CST
Baseline to Week 12

Mean Change in CST
At Week 12

% Patients ≤300 µm CST
At Week 12

Per Protocol population prior aflibercept subgroup (n=35), must have received all 3 intravitreal study treatments and evaluable at Baseline through Week 12 and sufficiently compliant with the protocol. Error bars (± SEM); Retinal Thickness measured by Spectral Domain-Optical Coherence Tomography (SD-OCT) as Central Subfield Thickness (CST)
## Safety

Well tolerated & consistent with previous OPT-302 Phase 1 and Phase 2b clinical trials in wet AMD

<table>
<thead>
<tr>
<th>Selected Adverse Events</th>
<th>Aflibercept (2mg) + Sham (N = 49)</th>
<th>Aflibercept (2mg) + OPT-302 (2 mg) (N =95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraocular inflammation</td>
<td>1 (2.0%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Cataract</td>
<td>1 (2.0%)</td>
<td>3 (3.2%)</td>
</tr>
<tr>
<td>Intraocular Pressure Increased^</td>
<td>3 (6.1%)</td>
<td>14 (14.7%)</td>
</tr>
<tr>
<td>Non-fatal myocardial infarction</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Non-fatal stroke*</td>
<td>0 (0%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Vascular death</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Any other death</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

• A total of 299 intravitreal injections of OPT-302 (any dose) were co-administered with aflibercept (2 mg) in the Phase 1b/2a DME trial

---

Safety population (n=144); TEAEs reported through Week 12.

*Changes in IOP were transient and there were no sustained changes to post-treatment mean IOP values compared to baseline.

*Grade 3 cerebrovascular accident, 21 days following the second dosing of study products, participant was hospitalized. No evidence of occlusion of the great vessels. It was concluded that a CVA could not be ruled out however its location is unclear. The event was assessed as possibly related as it was confounded by the underlying diabetes mellitus, which is a risk factor for the event, as well as underlying bladder cancer as having potential to induce thrombotic events. Participant withdrew consent and was discontinued due to the event.
# Safety – Intraocular Inflammation – Study Eye (All OPT-302 Trials)

Incidence of intraocular inflammation similar to control

<table>
<thead>
<tr>
<th>Study Eye</th>
<th>OPT-302 Any dose</th>
<th>2.0 mg OPT-302</th>
<th>Sham + anti-VEGF-A control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=399</td>
<td>N=263</td>
<td>N=169</td>
</tr>
<tr>
<td>N Participants (%)</td>
<td>Inj=1,842</td>
<td>Inj=1,121</td>
<td>Inj=854</td>
</tr>
<tr>
<td>Intraocular inflammation¹</td>
<td>7 (1.8%)</td>
<td>3 (1.1%)</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>OPT-302-1001</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Uveitis with anterior chamber cell 1+ (6-10)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Uveitis with anterior chamber cell 2+ (11-20)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>OPT-302-1002</td>
<td>3</td>
<td>1</td>
<td>2²</td>
</tr>
<tr>
<td>Endophthalmitis with anterior chamber cell 1+ (5-10) and hypopyon</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vitritis</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anterior chamber cell, trace (1-4 cells)</td>
<td>1</td>
<td>1</td>
<td>2²</td>
</tr>
<tr>
<td>OPT-302-1003</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Iritis with keratic precipitates and anterior chamber cell 2+ (11-20)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Iritis with anterior chamber cell 2+ (11-20)</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Anterior chamber cell, 4+ (&gt;50 cells) associated with cataract extraction/intraocular lens implant and hyphema</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Safety population; TEAEs reported to Week 12 for OPT-302-1003

¹ AEs and considered to be indicative of intraocular inflammation, defined prior to database lock: Iritis, anterior uveitis/Iritis, anterior chamber cells, endophthalmitis, vitritis and mutton fat keratic precipitate on endothelium

² Observed during ophthalmic examination, but not reported as TEAEs
Our Pipeline Includes Co-Formulation & Opportunities in PCV, RVO

Co-Formulation

- Co-formulate OPT-302 with a VEGF-A inhibitor
  - A single injection to inhibit VEGF-A/C/D
  - Program to generate/acquire biosimilar VEGF-A inhibitor and co-formulate with OPT-302
  - Manufacture and advance co-formulation through IND-enabling safety/tolerability studies and to clinic
  - Builds pipeline with VEGF-C/D ‘trap’ strategy
- IND Filing est. 2H 2021

Polypoidal Choroidal Vasculopathy (PCV)

- Sub-type of wet AMD with vessel dilations in retina resembling polyps
  - Typically do not respond well to anti-VEGF-A therapies
- High prevalence in Asian countries
  - Between 23-54% of presumed wet AMD cases in Japan are PCV
  - 4-10% of presumed wet AMD cases in Caucasians are PCV
- In Opthea’s Phase 2b wet AMD trial:
  - Benefit of +6.7 letters at week 24 following OPT-302 combination therapy compared to ranibizumab alone
  - Almost 2-fold improvement in VA gain

Retinal Vein Occlusion

- Sight-threatening visual disorder caused by blockage of retinal vein/s carrying blood out of retina
- Macular edema is most common cause of vision loss in people who suffer from RVO
- Affects approx. 1.8 million people in US and EU
- >500,000 people in US and EU have macular edema secondary to RVO
- There remains significant unmet medical need despite availability of approved anti-VEGF-A therapies
- Only 30-40% of patients experience significant gains in visual acuity following anti-VEGF-A therapy
Opthea – Developing OPT-302 for Eye Diseases

- OPT-302 has broad development potential in a range of eye diseases, including wet AMD and DME
- Targets validated VEGF/VEGFR pathway and mechanism of escape from existing therapies that is differentiated to VEGF-A inhibitors and other agents in development; Pan-VEGF (A, C and D) inhibition may offer benefits that exceed the inhibition of VEGF-A alone
- Wet AMD & DME landscape includes only a limited number of novel combination therapies that may address the sub-optimal clinical responses that many patients experience on anti-VEGF-A therapies; majority of agents in development seeking to improve durability of VEGF-A inhibition rather than address deficiencies in EFFICACY with existing agents. OPT-302 may address both EFFICACY and DURABILITY

Wet AMD:
- OPT-302 met primary endpoint of a large 366 patient Phase 2b clinical trial: demonstrating superior vision gain in patients treated with OPT-302 combination therapy compared to standard of care alone (p = 0.0107)
- OPT-302 combination therapy increased visual acuity by a further +5.7 letters over Lucentis monotherapy in wet AMD patients with minimally classic and occult lesions, representing the majority (~80%) of wet AMD patients
- Informs design and analysis strategy for Phase 3 trials

DME:
- Positive clinical outcomes in Phase 1b/2a trial of OPT-302 in combination with aflibercept (Eylea®) in patients with persistent DME

Safety:
- OPT-302 has demonstrated favorable tolerability in combination with both ranibizumab (Lucentis) and aflibercept (Eylea)
- Administration of over 1,800 doses of OPT-302 to 399 patients with retinal disease, indicates that OPT-302 intravitreal injections are well tolerated, with the incidence of treatment-emergent adverse events comparable to anti-VEGF-A monotherapy in our clinical trials

Phase 3 for wet AMD & Pipeline Opportunities:
- Phase 2b trial results inform Phase 3 trial designs. Phase 3 trials to initiate early 2021. Incorporate two standard of care anti-VEGF-A therapies to maximize commercial opportunity and will investigate extended dosing duration from q4w to q8w dosing
- Co-formulation program ongoing and additional development opportunities in PCV and RVO