July 7, 2014

HEALTHCARE/BIOTECHNOLOGY

Stock Rating:

OUTPERFORM

12-18 mo. Price Target	$95.00
OPHT - NASDAQ	$40.93

3-5 Yr. EPS Gr. Rate	NM
52-Wk Range	$47.99-$22.61
Shares Outstanding	33.3M
Float	17.3M
Market Capitalization	$1,364.5M
Avg. Daily Trading Volume	421,069
Dividend/Div Yield	NA/NM
Book Value	$6.22
Fiscal Year Ends	Dec
2014E ROE	NM
LT Debt	NA
Preferred	NA
Common Equity	$207M
Convertible Available	No

EPS Diluted	Q1	Q2	Q3	Q4	Year	Mult.
2013A	(4.33)	(8.07)	(10.26)	(0.65)	(6.34)	NM
2014E	(0.64)A	(0.62)	(0.65)	(0.69)	(2.60)	NM
2015E	--	--	--	--	0.84	NM

Revenue ($/mil)	Q1	Q2	Q3	Q4	Year	Mult.
2013A	0.0	0.0	0.0	0.0	0.0	NM
2014E	0.0A	1.3	2.6	2.6	6.6	NM
2015E	--	--	--	--	140.5	NM

Ophthotech Corporation

Compelling Retinal Disease Play; Initiating with Outperform

SUMMARY

We are initiating coverage of Ophthotech with an Outperform rating and a $95 price target. We expect Ophthotech's PDGF inhibitor Fovista being developed for wet AMD to succeed in an ongoing Phase 3 program (data 2016), with FDA approval to follow in 2017. Our view is based on solid proof-of-concept from randomized Phase 2 data that showed clear benefits in combination with an approved VEGF inhibitor (standard of care). Upon commercialization, we see Fovista eventually capturing ~25%/~10% share of US/EU wAMD patients on anti-VEGFs and generating peak US/EU sales of ~$1.75B/$500M. Indications for Fovista beyond wAMD (not modeled) and proof-of-concept for Phase 2 asset Zimura (we do not value) could generate additional upside.

KEY POINTS

- **Fovista Efficacy De-Risked.** In a large (N=449) randomized Phase 2b trial, Fovista + Lucentis (VEGF inhibitor) generated statistically significant gains in visual acuity over Lucentis monotherapy at 6 months (10.6 vs 6.5 letters, p = 0.0190). Multiple secondary measures of vision gain also consistently favored Fovista patients (see Exhibit 4 inside).
- **Fovista Phase 3.** All 3 trials (2 Lucentis, 1 Eylea/Avastin, geared to support a broad label + any VEGF) mirror the Phase 2b and benefit from greater power (N=661) and longer duration (1 year). Our statistical work suggests a broad cushion for success even assuming an anti-VEGF control arm tracking Regeneron's VIEW1/VIEW2 trials (Exhibit 13).
- **Fovista Pipeline.** wAMD studies of Fovista in VEGF non-responders, treatment-naive patients, and subretinal fibrosis (end stage of wAMD leading to long-term visual loss) are being planned. Success in any of these areas could expand the wAMD market opportunity for Fovista. However, we need to see evidence of proof-of-concept (data 2015-2016) before modeling.
- **Zimura.** The C5 complement inhibitor is being developed for wAMD and the larger dry AMD market. Zimura showed dose-dependent effects on slowing geographic atrophy (hallmark of late-stage dry AMD) in Phase 2a, but the trial was uncontrolled. Data (2016) from a planned Phase 2/3 trial in dAMD could clarify Zimura's potential.

Stock Price Performance

Company Description

Ophthotech is a biotechnology company focused on the development and commercialization of novel therapeutics to treat eye diseases. The company's most advanced asset is Fovista, a PDGF inhibitor being tested in combination with anti-VEGF therapy for wet age-related macular degeneration (wAMD), a disease characterized by progressive retinal damage and vision loss.

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Investment Thesis

Exhibit 1

Wet AMD Quick Facts

US Prevalence	~2 million
Risk factors	Age (over 50), gender (women), race (Caucasian), AMD in other eye, family history, high BP, obesity
Changes in eye physiology	Abnormal blood vessel growth beneath retina that leaks fluid
Rate of onset	Typically rapid (over several days or weeks)
Signs and symptoms	Visual distortions, decreased central vision, decreased intensity or color brightness
Diagnosis method	Fluorescein angiography, optical coherence tomography
Standard of care	Anti-VEGF therapy (Avastin, Eylea, or Lucentis)

Sources: www.amd.org, www.mayoclinic.org, eyecenter.dukemedicine.org.

Exhibit 2

Vision Function Impact of Wet AMD

Source: http://www.lucentis.com/lucentis/visual_impact.html

Summary & Conclusions

We are initiating coverage of Ophthotech with an Outperform Rating and a $95 price target. Ophthotech is a biotech company developing drugs to treat serious eye diseases, with a primary focus on wet age-related macular degeneration (wAMD). The company's lead asset, Fovista, a PDGF (platelet-derived growth factor) inhibitor, is being evaluated in a large Phase 3 program to improve visual outcomes when dosed in combination with approved VEGF inhibitors (Lucentis, Eylea and Avastin off-label; see Exhibit 7 for trial design). Top-line data are anticipated in 2016. **Based on the strength of the Phase 2b data, we expect success across Fovista's Phase 3 trials.** Assuming FDA approval (2H17), we model Fovista capturing ~25%/~10% peak US/EU share of anti-VEGF-treated wAMD patients driven by first-mover advantage for the novel PDGF inhibitor class. **Key aspects of our thesis include:**

- **Unmet need persists in wAMD despite benefits of anti-VEGF therapy.** Despite improvements in vision seen in the Eylea and Lucentis Phase 3 approval trials (VIEW1, mean 7.9 letter gain at 2q8 dose; MARINA, mean 7.2 letter gain at 0.5q4 dose), long-term benefit of anti-VEGF therapy remains suboptimal. A minority of patients maintained visual acuity (38% of eyes legally blind) 7-8 years after intensive Lucentis, and approximately half exhibited neovascular leakage (54% of eyes) and/or fibrotic scarring (42% of eyes), suggesting a waning effect of anti-VEGF therapy with time.[1]

- **Fovista + Lucentis delivers strong efficacy.** In Ophthotech's Phase 2b trial, the Fovista combination gained 10.6 EDTRS letters vs. 6.5 for Lucentis monotherapy after 24 weeks on therapy in Phase 2b. The majority of the retinal specialists we consulted considered a ~4 line improvement as clinically relevant in wAMD.

- **Phase 3 design de-risked, and with some improvements over Phase 2b.** Reproducing the Phase 2 design in Phase 3 eliminates a source of risk in the critical Phase 2 to Phase 3 transition where many drugs have stumbled. Longer duration (1-year in Phase 3 vs 24 weeks in Phase 2b) may provide an opportunity to realize potential additional benefits of Fovista in a time frame (6 months to 1 year) where efficacy of anti-VEGF monotherapy appeared to plateau (see Exhibit 12, Eylea vs. Lucentis head-to-head trials). Higher power (662 patients per trial vs. 445 in Phase 2b) is another plus (see next bullet). While Fovista + Eylea and Fovista + Avastin were not tested in Phase 2b, we see limited risk to using a different VEGF inhibitor in a third Phase 3 trial given a shared mechanism (recall Lucentis is a molecular fragment of Avastin).

- **High likelihood of hitting Phase 3 endpoints per our statistical work.** Given higher powering, a reproduction of the Phase 2b benefit in Phase 3 would drive strong statistical significance (see Exhibit 10, $p = 6.8 \times 10^{-5}$). However, the performance of Lucentis in the Phase 2b may be weak relative to historical data. If Fovista's Phase 3 control arms follow Regeneron's VIEW1 and VIEW2 trials and Fovista's Phase 2b efficacy at 24 weeks (10.6 letters) continues to build over months 6-12, the trials should still generate overwhelmingly statistical significance (see Exhibit 12, $p = 4.6 \times 10^{-15}$ and Exhibit 13, $p = 3.4 \times 10^{-6}$).

- **Solid Phase 2 to Phase 3 Read-through in wet AMD.** The development history of approved wet AMD drugs Eylea and Lucentis supports good translatability of Phase 2 efficacy to Phase 3 (see Exhibit 17 and Exhibit 18). In fact, Phase 3 efficacy for Lucentis substantially improved vs. Phase 2.

- **Modest share projections (~25%) enough to support our valuation.** Our discussions with retinal specialists who treat wAMD consistently cited ~25% as the proportion of practice patients where additional efficacy with a second drug

[1] SEVEN UP observational study that followed 63 patients who participated in the MARINA/ANCHOR and HORIZON trials of Lucentis, *Ophthalmology*. 2013; 120: 2292–2299.

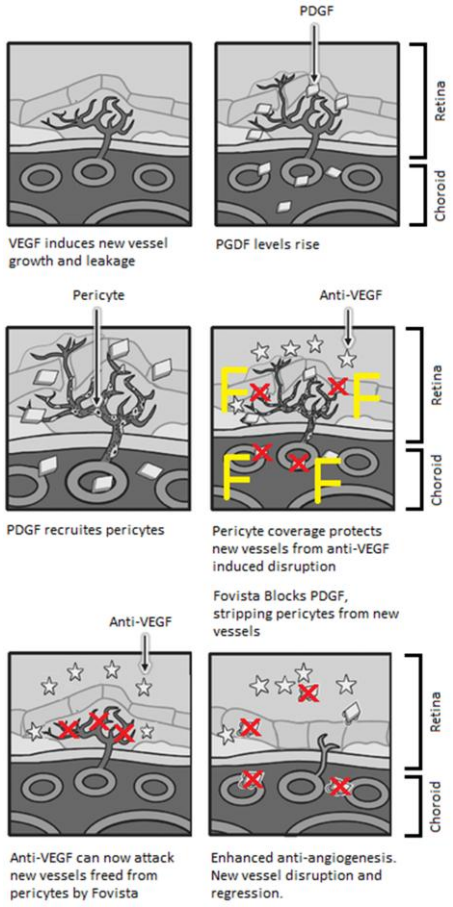
(i.e., Fovista) would be immediately desirable. Physicians offered these views based on knowledge of the Phase 2b data set's efficacy and safety, an assumption on price we provided ($1450/injection) and an understanding that a second injection would be required.

- **EU share projection (~10%) also supports our target, but this may prove conservative with Novartis running commercialization in EU.** We have assumed a ~10% peak blended share across anti-VEGF-treated patients in the EU, based on limited reimbursement prospects in Europe for potentially costly combination therapies, as well as higher EMA risk around the Eylea/Avastin Phase 3 (EMA is concerned Fovista has never been tested previously with either drug). We would expect Novartis to push hard for combination with Lucentis (still holds ~45% EU share in wAMD post Eylea launch), so our assumed ~18% peak Lucentis share for Fovista may be light.

- **Fibrosis hypothesis could offer long-term upside to Fovista adoption.** Retrospective imaging analysis from Ophthotech's Phase 2b trial suggests Fovista may ameliorate subretinal fibrosis, believed to contribute to poor long-term visual acuity in wAMD. If positive, randomized data (late 2015 / early 2016) supporting Fovista's benefits in fibrosis could provide a step-up in the adoption curve upon launch.

Exhibit 3

Fovista Mechanism of Action in wAMD in Promoting Neovascular Regression



Sources: Ophthotech Reports, Oppenheimer Research. F = Fovista.

Wet AMD Unmet Need Persists

There remains a significant unmet need in wet AMD for therapies that can 1) enhance visual acuity, 2) maintain vision or 3) delay visual decline. See Appendix I, p. 26 for AMD background.

wAMD patients can lose vision quickly even with anti-VEGF therapy. After one year of treatment with an anti-VEGF drug, 18-22% of newly diagnosed wet AMD patients had lost additional vision.

Vision loss is common and vision gains are transient even with extended anti-VEGF therapy. Forty-six percent of patients treated for two years with an anti-VEGF in clinical trials who then received additional anti-VEGF at physician's discretion for another two years had lost additional vision. In a four-year longitudinal study of 555 wAMD patients treated with Lucentis, mean visual acuity returned to pre-study levels, and 28% discontinued, citing sustained low visual acuity and ineffective response.[2]

Longer term outcomes appear dismal. Seven to eight years after intensive Lucentis, a minority of patients maintained visual acuity (38% of eyes legally blind), and approximately half exhibited neovascular leakage (54% of eyes) and/or fibrotic scarring (42% of eyes), suggesting a waning effect of anti-VEGF therapy with time.[3]

Meaningful fraction of patients never respond to anti-VEGF. Ten to thirty percent of wAMD patients do not appear to respond to anti-VEGF therapy.

Fovista Phase 2b – Strong Efficacy

Ophthotech's Phase 2b trial met the primary endpoint showing a ~62% benefit in visual acuity for Fovista + Lucentis over Lucentis. The mean change in visual acuity from baseline at 24 weeks (as measured by ETDRS letters) was +10.6 letters for the high-dose (1.5 mg) Fovista arm vs. +6.5 letters for Lucentis alone, with a p-value of 0.0190.

In the trial, 449 treatment-naïve wAMD patients were randomized 1:1:1 to 0.3 mg Fovista + Lucentis vs. 1.5 mg Fovista + Lucentis vs Lucentis monotherapy (445 were evaluable for efficacy). Lucentis was injected first, followed by Fovista after a 30-minute gap to allow for equilibration of intra-ocular pressures. Lucentis monotherapy patients received a sham injection to maintain blinding.

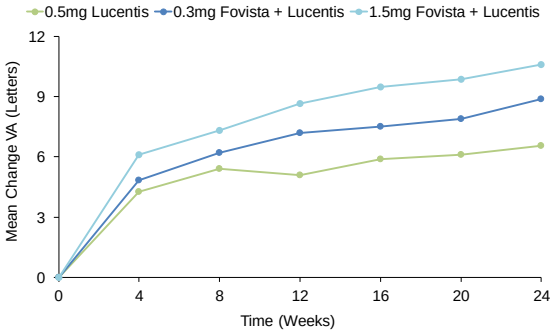
[2] *Ophthalmology*. 2013; 120: 2630-2636

[3] SEVEN UP observational study that followed 63 patients who participated in the MARINA/ANCHOR and HORIZON trials of Lucentis, *Ophthalmology*. 2013; 120: 2292–2299.

Although the trial showed a clear dose response across all time points measured, the lower 0.3 mg Fovista arm (8.8 letter gain) was not statistically different from Lucentis (see Exhibit 4), so 1.5 mg was selected for further development. **We note that dose response is not linear (a 5x higher dose roughly only doubles the visual gains), which may raise some eyebrows, but a sub-linear response, particularly on a complex neurological measure like vision, does not seem unusual to us.** Separately, some have observed that the Lucentis arm performed below historical expectations for Lucentis (~9-10 letters in HARBOR and ~10 letters in ANCHOR at 6 months; on the other hand, MARINA was only ~6 letters at 6 months), but such a cross-trial comparison carries little weight in our view relative to the value of a controlled, randomized study.

Exhibit 4

Fovista Phase 2b Trial Meets Primary Endpoint



Sources: Ophthotech Reports, Oppenheimer Research.

Exhibit 5

ETDRS Eye Chart

Source: www.sussexvision.co.uk

Secondary endpoints provide a consistent picture of efficacy favoring Fovista. A range of additional measures examining the proportion of patients with gains of > 3, > 4 and > 5 lines (5 letters per line on ETDRS chart) and losses of ≥ 1 or ≥ 2 lines continued to reflect an advantage for Fovista + Lucentis. Systematic success on these secondary endpoints argues that Fovista is providing benefit to wAMD patients across a wide range of underlying responses to anti-VEGF therapy. This feature of the Phase 2b data seems to provide good clinical support for Fovista's independent mechanism (vs. anti-VEGFs) in driving visual gains by stripping pericytes from blood vessels (see Exhibit 3 for Fovista mechanism). Overall, we see the Phase 2b data as providing clear proof-of-concept for Fovista in wAMD within the rigorous framework of a randomized, controlled, double-blind trial.

Exhibit 6

Consistent Pattern of Efficacy Favoring Fovista in Phase 2b Trial

	1.5 mg Fovista + Lucentis	0.3 mg Fovista + Lucentis	0.5 mg Lucentis
Mean Change in VA (Baseline at 24 Weeks)	10.6 (N=151)	8.8 (N=147)	6.5 (N=147)
Visual Gain at 24 Weeks (% of Patients):			
More than 3-Line Gain	*36.4% (N=55)*	-	*28.6% (N=42)*
More than 4-Line Gain	*19.9% (N=30)*	-	*11.6% (N=17)*
More than 5-Line Gain	*11.9% (N=18)*	-	*4.1% (N=6)*
20/40 or Better	*37.0% (N=54)*	-	*31.9% (N=46)*
20/25 or Better	*12.3% (N=18)*	-	*5.6% (N=8)*
Visual Loss at 24 Weeks (% of Patients):			
1-Line or More	*8.3% (N=12)*	-	*21.5% (N=31)*
2-Line or More	*3.4% (N=5)*	-	*12.5% (N=18)*
20/200 or Worse	*10.3% (N=15)*	-	*13.9% (N=20)*
Mean Change in Area of CNV at 24 Weeks (Disk Area)			
Small CNV ≤1.62 DA	*-0.12 (N=104)*	-	*-0.06 (N=84)*
Large CNV >1.62 DA	*-1.73 (N=43)*	-	*-1.59 (N=60)*
Mean Change in Area of CNV at 24 Weeks in Patients with Visual Gain of More Than 3-Lines (Disk Area)			
Small CNV ≤1.62 DA	*-0.10 (N=43)*	-	*-0.01 (N=32)*
Large CNV >1.62 DA	*-2.33 (N=10)*	-	*-0.24 (N=10)*
Presence of Subretinal Hyper-Reflective Material at Baseline (% of Patients)			
All Patients	*92.8% (N=141)*	-	*93.2% (N=138)*
Patients With Significant Gain (>3-Lines)	*87.3% (N=48)*	-	*90.5% (N=38)*
Absence of Subretinal Hyper-Reflective Material at Week 24 (% of Patients)			
All Patients	*32.4% (N=47)*	-	*21.5% (N=31)*
Patients With Significant Gain (>3-Lines)	*53.8% (N=28)*	-	*38.1% (N=16)*

Sources: Ophthotech Reports, Oppenheimer Research.

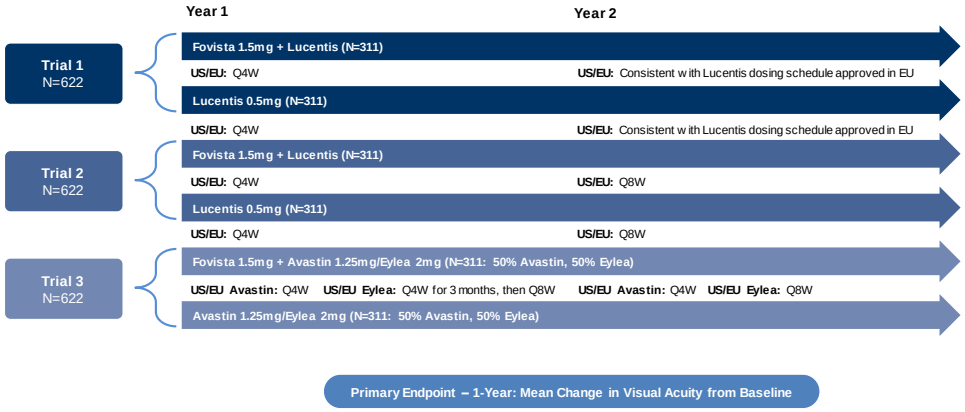
The safety profile for Fovista in the Phase 2b trial was generally unremarkable. Conjunctival hemorrhage (33.6% for 0.5 mg Fovista vs. 25% for Lucentis), eye pain (8.6% for 0.5 mg Fovista vs. 5.4% for Lucentis) and high intraocular pressure (5.9% for 0.5 mg Fovista vs. 2.7% for Lucentis) were the main standouts. Our physician diligence considered slightly higher frequencies for these side effects as acceptable and understandable given a second injection into the eye. Additionally, they tend to resolve quickly and do not pose any long-term risks to ocular health. There were no cases of eye infection (endophthalmitis). Relatedly, Macugen (the first approved anti-VEGF) was also a PEGylated aptamer (RNA) with good safety characteristics, providing some precedent for Fovista's expected acceptable safety profile in larger trials (Fovista is also an aptamer, albeit DNA-based).

Fovista Phase 3 Program

Overall, the consistency in design between Phase 2b and the Phase 3 program tends to minimize clinical risk, especially for the Lucentis trials. Moreover, higher power and longer duration for the primary endpoint seem to be new advantages in the Phase 3 design (discussed in more detail below; see Statistical Deep Dive, p. 6). Ophthotech is enrolling three Phase 3 trials as a basis for regulatory approvals in the US and EU. Enrollment commenced in August 2013 and > 225 centers worldwide are participating. The first two trials (N = 622 each) are replicates and, like the Phase 2b, are comparing Fovista 1.5mg + Lucentis to Lucentis monotherapy. A third trial (also N = 622) uses the same overall design but is testing Eylea or Avastin as the backbone VEGF, wherein each arm patients will be sub-randomized 1:1 to Eylea or Avastin (see Exhibit 7). The patient population for all three Phase 3 studies (treatment-naïve subfoveal choroidal neovascularization (CNV) from wAMD with some classic component) is identical to the Phase 2b. The primary endpoint measurement (mean change in visual acuity (ETDRS letters) from baseline) is also the same, but in the Phase 3 will be evaluated at a longer 12 months (vs. 6 months). Additionally, the dosing schedule is reproduced (every 4 weeks through 12 months) and the spacing between injections (Fovista 30 minutes after the anti-VEGF) remains fixed from Phase 2b to Phase 3. Last, the Phase 3 trials will each enroll 622 patients vs. 449 for the Phase 2b, offering more power to detect a statistically significant signal.

Exhibit 7

Fovista Phase 3 Program in wAMD



Sources: Ophthotech Reports, Oppenheimer Research. Under certain circumstances suggesting visual decline (> 5 decrease in ETDRS or negative findings on fluorescein angiography or SD-OC), treatment at the alternate month visit is permitted on the Q8W schedule.

The most obvious source of risk for the Phase 3 program is the third trial with Eylea/Avastin because Fovista has not been tested in combination with these agents in prior human trials, but the antibody science and clinical trial data seem to cap this risk as well. Lucentis is a fragment of the larger Avastin antibody, and clinical effectiveness is comparable based on data from the CATT trial (*New England Journal of Medicine* 2011, 364 (20): 1897–1908), so we would expect similar behavior for Fovista + Avastin as Fovista + Lucentis. On the other hand, Eylea is a ~100-fold more potent VEGF binder (0.36 pM) than either Avastin (58 pM) or Lucentis (46 pM) (see *Angiogenesis*. June 2012; 15(2): 171–185) and is being dosed every 4 weeks (Q4W) for the first 3 months of

Ophthotech's trial and then every 8 weeks (recall the Eylea label specifies 3 injections over 3 months and then only every other month). **These factors seem to suggest that Eylea may offer higher baseline efficacy on visual gains, which theoretically could leave less room for Fovista to show an added benefit.** However, we admit this statement is speculative because although we have some indication from the Phase 2b that Fovista is working over a range of underlying responses to anti-VEGF, we lack a full understanding of whether 1.5 mg Fovista delivers:

1) An absolute (or proportional) additional visual benefit over anti-VEGF therapy

2) Additional efficacy only at or below some minimal threshold of baseline visual gain on anti-VEGF, or

3) Efficacy benefits that diminish as baseline anti-VEGF efficacy rises (above speculation).

Future data disclosures from Ophthotech's Phase 2b trial, such as the average letters gained for Lucentis vs Fovista 1.5 mg among patients gaining ≥ 25 letters, could shed some light on these issues. Of course, the much larger Phase 3 data set (1,866 patients) should provide significant insight into how Fovista's benefits are manifest in relation to underlying anti-VEGF efficacy.

Regardless, integrated 52-week data from Regeneron's Phase 3 VIEW1 and VIEW2 trials showed that Q4W Eylea performed similarly (+9.3 letters) vs. Q8W Eylea (8.4 letters) and vs. Lucentis Q4W (8.7 letters), suggesting our theoretical concern may not be valid. Moreover, even if Eylea Q4W performs atypically well (in VIEW1 the difference was more pronounced at 10.9 letters for Eylea Q4W vs. 8.1 and 7.9 for Lucentis Q4W and Eylea Q8W, though trends were just the opposite in VIEW2), we suspect that **1)** Eylea Q4W for only 3 months and **2)** the contribution of Avastin to the VEGF backbone efficacy could buffer the overall analysis. In addition to possible cost considerations, lumping Avastin and Eylea into one trial may have been a risk-mitigation strategy on Ophthotech's part to avoid an isolated comparison of Fovista + Eylea vs. Eylea on a primary endpoint. In any event, the Eylea/Avastin trial could be viewed as two smaller trials merged (i.e., N=311 each for Fovista + Avastin vs. Avastin and Fovista + Eylea vs. Eylea). **Therefore, in addition to the overall analysis, we would expect data disclosure for each stratum that could provide independent windows into Fovista's performance + Eylea and + Avastin, which of course will have important commercial implications.**

Fovista Phase 3 – Statistical Analysis Deep Dive

We expect success in the Fovista Phase 3 program, supported by the strength of the Phase 2b data, Fovista's mechanism of action and our proprietary statistical analysis of the hurdle for a positive trial across a range of assumptions for the control arm and corresponding bull, base and bear scenarios for the Fovista arm. For the anti-VEGF control arm, we have examined three broad scenarios:

1) Anti-VEGF control arm behaves like Phase 2b.

2) Anti-VEGF control arm behaves like the integrated data from Regeneron's VIEW1 and VIEW2 trials (Lucentis and Eylea H2H).

3) Anti-VEGF control arm behaves like data from the CATT trial (Lucentis and Avastin H2H).

We believe our analysis has merit across all the anti-VEGFs (even though only Lucentis was studied in Phase 2b) given broad mechanistic equivalence among Eylea, Lucentis and Avastin supported by clinical data and physician experience.

Scenario 1: Anti-VEGF control arm behaves like Phase 2b

Bull Case: The trajectory of widening benefit seen in Phase 2b continues to build over time through week 52 (Exhibit 9) based on a linear extrapolation of the Phase 2b slopes over weeks 4-24. The p-value for this scenario (1.4×10^{-13}, Student t-test (2-tailed) for difference between means; see Appendix II p. 22 for details) is overwhelmingly significant based upon **1)** higher power and **2)** a more pronounced treatment effect over time.

Exhibit 8

Key Conclusions from Statistical Analysis of Fovista Phase 3 Program

(see text for details)

Scenario 1

	Fovista	Anti-VEGF
Bull	Efficacy Builds at Phase 2b rate	Efficacy Builds at Phase 2b rate
Base	Fovista Flat	Anti-VEGF Flat
Bear	Fovista Flat	Efficacy Builds at Phase 2b rate

Scenario 2

	Fovista	Anti-VEGF
Bull	Efficacy Builds at Phase 2b rate	VIEW1 and VIEW2
Base	Efficacy Builds at ~50% Phase 2b rate	VIEW1 and VIEW2
Bear	Fovista Flat	VIEW1 and VIEW2

Scenario 3

	Fovista	Anti-VEGF
Bull	Efficacy Builds at Phase 2b rate	CATT Trial
Base	Efficacy Builds at ~50% Phase 2b rate	CATT Trial
Bear	Fovista Flat	CATT Trial

Statistically Significant

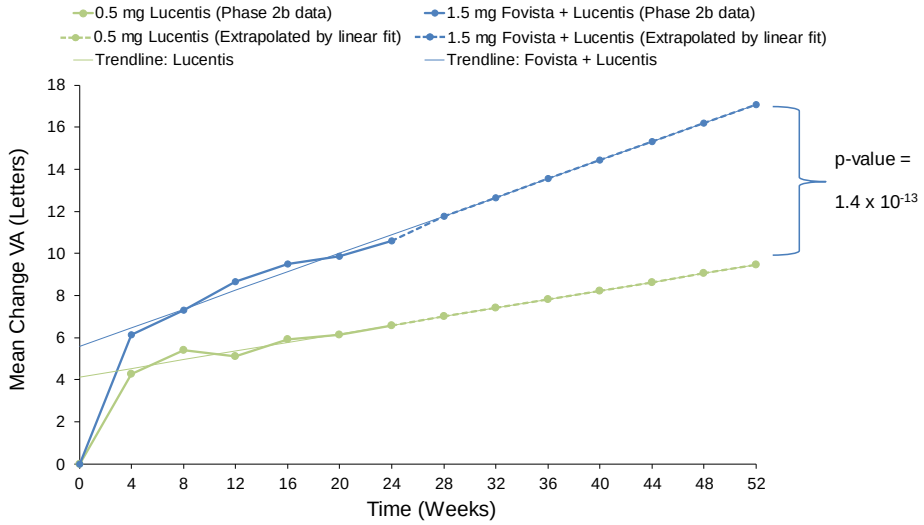
Not Statistically Significant

Source: Oppenheimer Research.

Base Case: The benefit seen in the Phase 2b at week 24 remains stable over time through week 52 for both arms. The p-value for this scenario (6.8 x 10^{-5}, Student t-test (2-tailed) for difference between means) is greater than in Phase 2b (p = 0.0190), as would be expected based on **1)** higher power and **2)** no penalty for multiple comparisons (recall in Phase 2b the Hochberg procedure for multiple comparisons among the three arms likely diluted the p-value).

Exhibit 9

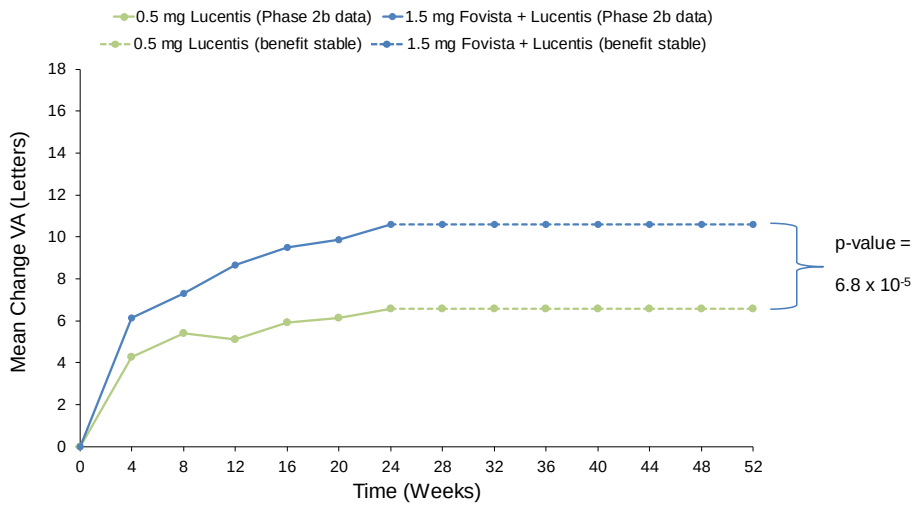
Bull Case: Fovista's Widening Treatment Benefit Builds with Time over Weeks 24-52



Sources: Ophthotech Reports, Oppenheimer Research

Exhibit 10

Base Case: Fovista and anti-VEGF Remain Stable over Weeks 24-52

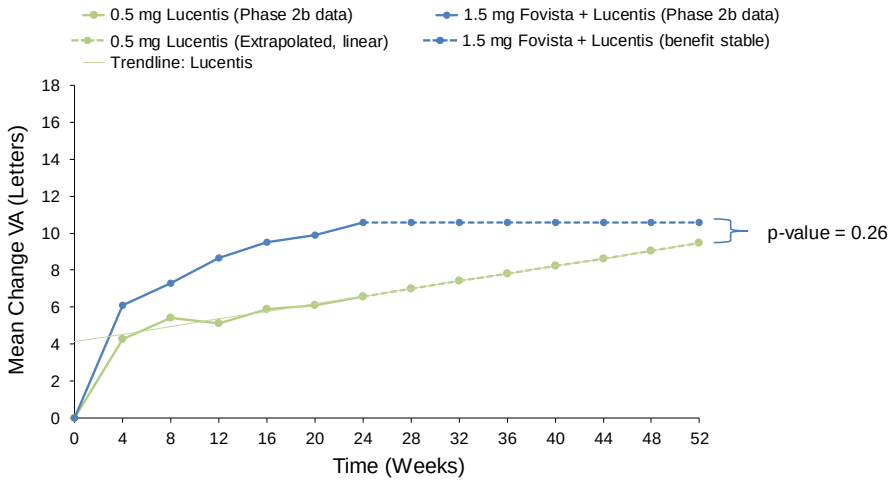


Sources: Ophthotech Reports, Oppenheimer Research

Bear Case: The benefit seen in the Phase 2b at week 24 remains fixed over time through week 52 for the Fovista arm, but efficacy in the anti-VEGF arm continues to build linearly as per Exhibit 9. The p-value for this scenario (0.26, Student t-test (2-tailed) for difference between means) is non-significant. **We view this outcome as unlikely** because it suggests **1)** the benefits of Fovista wane with time, which the current evidence does not support and conversely, **2)** the benefits of anti-VEGF build with time over weeks 24-48, a trend which is also not supported by several large Phase 3 trials in wAMD (see discussion below and Exhibit 12).

Exhibit 11

Bear Case: Fovista's Efficacy Remains Stable through Week 52, anti-VEGF Continues to Deliver Benefit



Sources: Ophthotech Reports, Oppenheimer Research

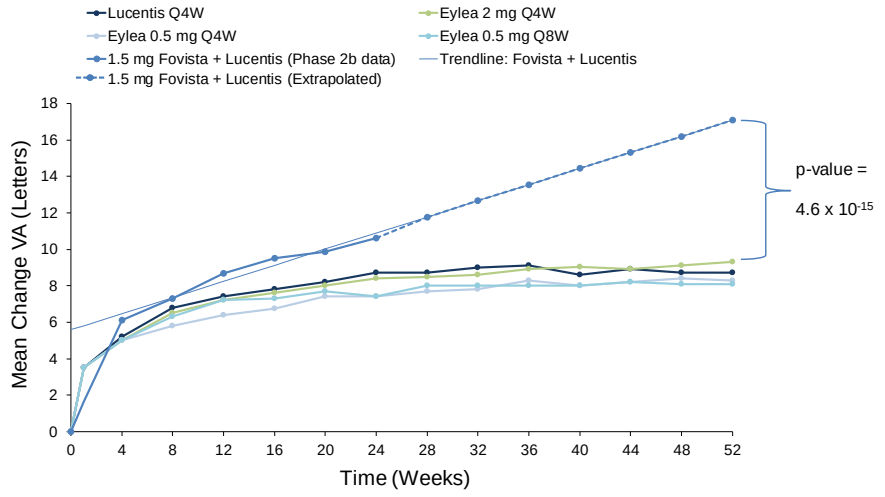
Scenario 2: Anti-VEGF Control Arm Behaves Like the Integrated Data from Regeneron's VIEW1 and VIEW2 trials (Lucentis and Eylea Head-to-Head).

As discussed earlier, the Lucentis performance in the Phase 2b may be on the lower end of Lucentis efficacy historically. Given this, we assumed in Scenario 2 that the anti-VEGF control arm in Ophthotech's Phase 3 program behaves like the integrated data from Regeneron's VIEW1 and VIEW2 pivotal trials.[4] Importantly, VIEW1 and VIEW2 provide solid evidence that benefits of anti-VEGF therapy in terms of letters gained appear to plateau at ~24 weeks (Exhibit 12).

Bull Case: The trajectory of benefit seen in Phase 2b for Fovista continues to build over time through week 52 (Exhibit 12) based on a linear extrapolation of the Phase 2b slopes over weeks 4-24. The control arm mirrors the pooled VIEW1 and VIEW2 data. The p-value for this scenario is 4.6×10^{-15}, Student t-test (2-tailed) for difference between means.

Exhibit 12

Bull Case: Fovista's Treatment Benefit Builds with Time over Weeks 24-52, anti-VEGF Behaves Like VIEW1 and VIEW2



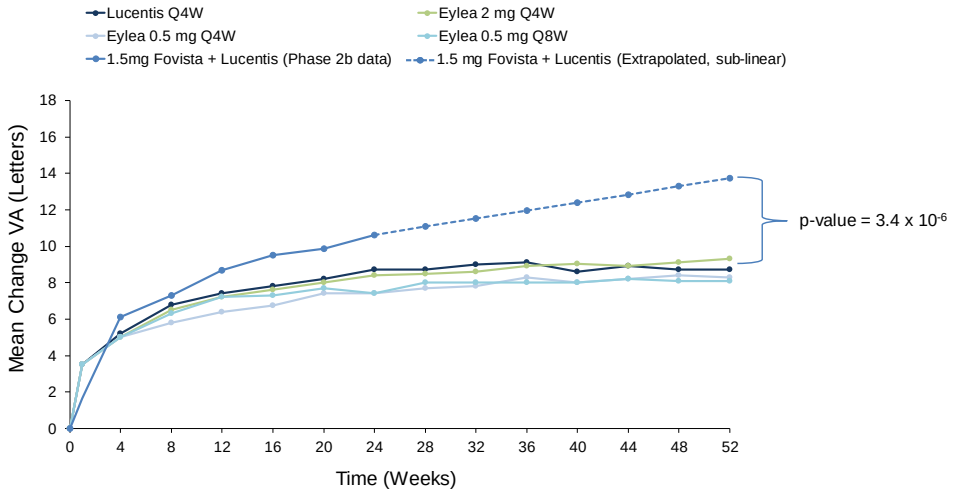
Sources: Ophthotech Reports, Oppenheimer Research, *Ophthalmology* 2012;119:2537–2548.

[4] In VIEW1 and VIEW2, we used the average value of 9.0 letters gained at 52 weeks for the Lucentis Q4W arm and the Eylea 2mg Q4W arm, excluding the Q4W 0.5 mg arm and the Q8W 2 mg arm.

Base Case: The benefits seen in Phase 2b for Fovista continue to build over time through week 52 **but more modestly relative to the initial slope over weeks 0-24 (see Exhibit 13).** Again, the control arm mirrors the pooled VIEW1 and VIEW2 data. The p-value for this scenario is 3.4 x 10^{-6} (Student t-test (2-tailed) for difference between means).

Exhibit 13

Base Case: Fovista's Treatment Benefit Builds More Modestly with Time over Weeks 24-52, anti-VEGF Behaves Like VIEW1 and VIEW2

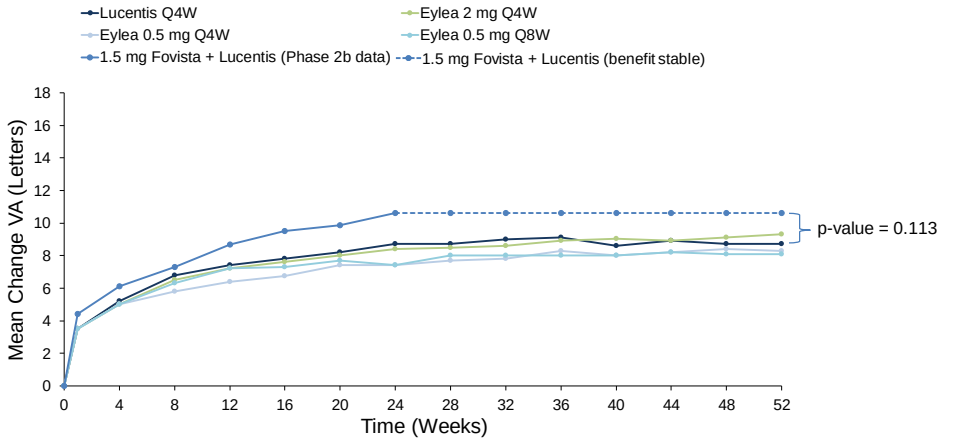


Sources: Ophthotech Reports, Oppenheimer Research, *Ophthalmology* 2012;119:2537–2548.

Bear Case: The benefit seen in the Phase 2b at week 24 remains fixed over time through week 52 for the Fovista arm (Exhibit 14). The control arm mirrors the pooled VIEW1 and VIEW2 data. The p-value for this scenario is 0.113 (Student t-test (2-tailed) for difference between means). The trial lacks power to detect a ~2 letter benefit over the anti-VEGF arm, which suggests to us the right level of investment in the study. Higher powering to lock-in significance on a ~2 letter benefit might win an approval but would be unlikely to be met with much clinical enthusiasm. **Regardless, we see this outcome as unlikely.**

Exhibit 14

Bear Case: Fovista's Efficacy Remains Stable through Week 52, anti-VEGF Behaves Like VIEW1 and VIEW2



Sources: Ophthotech Reports, Oppenheimer Research, *Ophthalmology* 2012;119:2537–2548.

<u>Scenario 3: Anti-VEGF Control Arm Behaves Like Data from the CATT trial (Lucentis and Avastin H2H).</u>

Our conclusions mirror Scenario 2. Based on similar assumptions for Fovista as in Scenario 2, our bull / base / bear cases yield p-values of 1.5 x 10^{-17} / 8.1 x 10^{-8} / 0.02,

respectively. In the CATT trial, 8.25 letters were gained on average at week 52 for Lucentis Q4W and Avastin Q4W in the CATT.

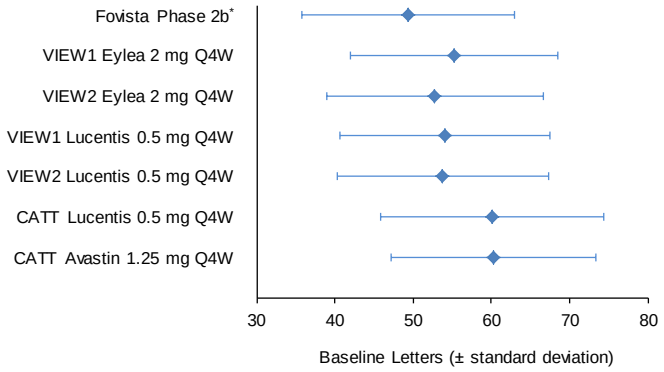
Overall, we see our base case (with a focus on Scenario 2) as a fair proxy for the potential efficacy that Fovista can deliver over anti-VEGF over weeks 24-52 in Phase 3, generating a highly statistically significant outcome.

However, there are two important assumptions in our analysis worth highlighting:

1) Baseline visual acuity is approximately equivalent across trials. We believe comparing the Fovista Phase 2b vs. VIEW1/VIEW2 and vs. the CATT trial on roughly equal footing in terms of letters of vision gained is an acceptable assumption given approximately equivalent baseline visual acuity across the three trials (Exhibit 15).

Exhibit 15

Baseline Visual Acuity Across Fovista Phase 2b, VIEW1/VIEW2 and CATT Trials Support Comparability of Patient Populations



Sources: Ophthotech Reports, Oppenheimer Research, *N Engl J Med* 2011;364:1897-908, *Ophthalmology* 2012;119:2537–2548. * Ophthotech did not disclose the standard deviation associated with the mean baseline letters of 49.3 for the Fovista 1.5 mg arm. We used the average standard deviation for the other trials cited (± 13.6) to approximate the standard deviation for Fovista, which we recognize is an approximation, though a plausible one.

2) Standard deviation (SD) of the mean letters of vision gained in Phase 3 is approximately equivalent across drugs. This may appear technical but should not be overlooked. SD is a key ingredient that drives the statistics (Student t-test) when comparing two means. Importantly, Ophthotech has indicated that the error bars (95% confidence intervals) for the Fovista 1.5 mg and the Lucentis arms in the Phase 2b trial do not overlap. We therefore assume conservatively the maximum non-overlapping distance of 2 letters, implying a 95% confidence interval (CI) of [8.6,12.6] for Fovista 1.5 mg. Using the conversion

$$\text{Standard Deviation} = \sqrt{Sample\ Size}\ x \left[\frac{Upper Limit\ 95\%\ CI - Lower\ Limit\ 95\%\ CI}{2(1.96)}\right]$$

the standard deviation is 12.6 letters. As a quick cross-check, in VIEW1 / VIEW2 the standard deviations for the Eylea 2 mg Q4W arm are a similar 13.8 / 12.6 letters and for the Lucentis 0.5 mg Q4W arm 15.3 / 13.5 letters, respectively, so the Fovista Phase 2b is in the right neighborhood.

As an additional cross-check, we explored a range of standard deviations larger than 12.6 in a sensitivity analysis (see Exhibit 16) that could negatively impact our conclusions on the probability of success in the base case for Scenario 2 (recall that higher SDs create more noise, setting up a higher hurdle for statistical significance). **Our conclusions are generally robust with respect to choice of standard deviation even for a 2.3-fold increase (SD = 28) for both arms**, and either arm's SD can reach 36 with the corresponding arm's SD = 20 and still be within $p < 0.05$.

Exhibit 16

Our Conclusion on Statistical Significance for Our Base Case (Scenario 2) Is Robust with Respect to Standard Deviation Assumed (Sensitivity Analysis)

SD Lucentis + Fovista \ SD Lucentis	12	16	20	24	28	32	36
12	1.196E-06	3.602E-05	3.863E-04	2.009E-03	6.466E-03	1.515E-02	2.864E-02
16	3.602E-05	2.549E-04	1.217E-03	4.040E-03	1.008E-02	2.031E-02	3.501E-02
20	3.863E-04	1.217E-03	3.373E-03	7.914E-03	1.585E-02	2.776E-02	4.369E-02
24	2.009E-03	4.040E-03	7.914E-03	1.446E-02	2.435E-02	3.785E-02	5.483E-02
28	6.466E-03	1.008E-02	1.585E-02	2.435E-02	3.595E-02	5.073E-02	6.846E-02
32	1.515E-02	2.031E-02	2.776E-02	3.785E-02	5.073E-02	6.635E-02	8.446E-02
36	2.864E-02	3.501E-02	4.369E-02	5.483E-02	6.846E-02	8.446E-02	1.026E-01

Source: Oppenheimer Research; Green regions indicate p < 0.05.

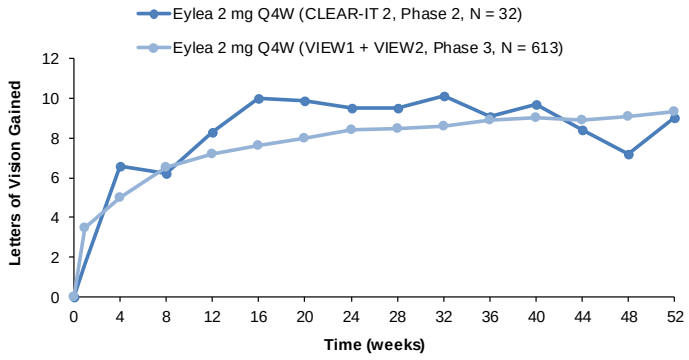
Phase 2 to Phase 3 Read-through in wet AMD Looks Solid

Prior development efforts for Eylea and Lucentis suggest Phase 2 efficacy provides a good proxy for Phase 3 data in wet AMD, adding another layer of support to our thesis on Fovista and Ophthotech.

Eylea Phase 2 to Phase 3 Transition. Change in visual acuity for the 2 mg Q4W schedule (N = 32) in Eylea's 1-year Phase 2 trial (CLEAR-IT 2) overlaps well with the pooled change in visual acuity data (N = 613) for Eylea's VIEW1 and VIEW2 pivotal trials (2 mg Q4W) (Exhibit 17). Some may argue that in CLEAR-IT 2, dosing post 12 weeks was as needed (i.e., pro re nata, PRN), whereas in VIEW1/VIEW2 Eylea dosing was Q4W for the full 52 weeks, suggesting Phase 3 efficacy may be slightly *worse* than Phase 2 given approximate overlap. However, the relatively noisy and small (N = 32) Phase 2 dataset vs. VIEW1/VIEW2's ~600 blunts this argument in our view.

Exhibit 17

Eylea Development Supports Good Phase 2 to Phase 3 Efficacy Read-through in wet AMD

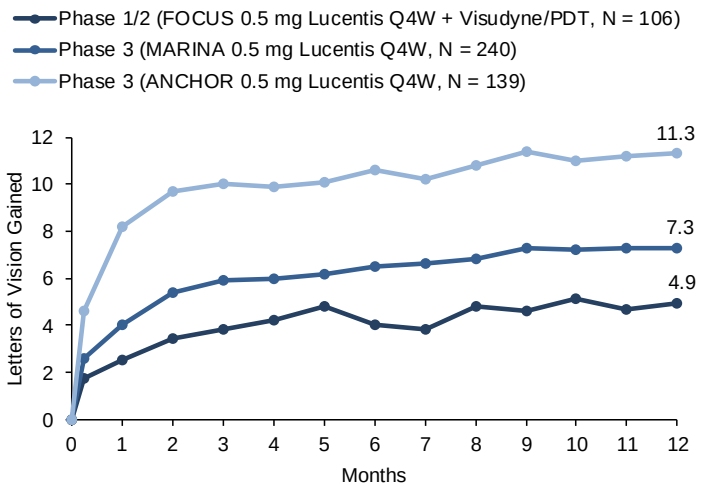


Source: Oppenheimer Research; 2008 Retina Society Meeting CLEAR-IT 2 presentation; *Ophthalmology* 2012;119:2537–2548.

Lucentis Phase 2 to Phase 3. A similar theme emerges for Novartis's anti-VEGF. Interestingly, there is a substantial step-up in Phase 3 efficacy in the MARINA and ANCHOR trials vs. the earlier Phase 2 FOCUS trial (Exhibit 18). Recall, FOCUS included photodynamic therapy, so the comparison is not ideal. However, the typical investor concern is that Phase 2 can *overestimate* Phase 3 and in FOCUS a retrospective comparison vs. ANCHOR and MARINA suggests photodynamic therapy may have worked against Lucentis. **Regardless, we believe we can safely conclude from our overlay analysis that Lucentis' Phase 2 efficacy did not overstate Lucentis' Phase 3 performance.**

Exhibit 18

Lucentis Development Supports Good Phase 2 to Phase 3 Efficacy Read-through in wet AMD



Source: Oppenheimer Research; *Arch Ophthalmol.* 2006;124:1532-1542, *N Engl J Med* 2006;355:1419-31, *Ophthalmology* 2009;116:57–65.

Thoughts on Fovista Phase 3 Outcomes and the Label

Here is how we see the Phase 3 program playing out at a trial-by-trial level:

- **All three Phase 3 trials work (our base-case expectation).** We see a clear path to approval by the FDA and EMA. We would expect a broad label in the US enabling Fovista combination with any VEGF-inhibitor (implicitly including Avastin despite no formal label in wAMD) that is not restricted to newly diagnosed wAMD. In the EU, because Avastin is not approved for intravitreal applications, the EMA label may be restricted to approved anti-VEGF therapies Lucentis and Eylea. However, we have already accounted for this scenario in our base-case share assumptions as we only grant Fovista a ~5% peak share of Avastin-treated wAMD patients in the EU.

- **Both Lucentis trials work, but the Eylea/Avastin trial fails (bear-case 1).** We continue to expect US approval, though the breadth of the label may be restricted to Lucentis pending some post-marketing work to broaden the label to "any VEGF therapy." In the EU, a failed Eylea/Avastin trial would also seem to imply a Lucentis-only label at the outset. Further post-marketing work could add Eylea to the label, but, as indicated above, a label spanning "any anti-VEGF" may be an unrealistic expectation in the EU.

- **Only one Lucentis trial works, and the Eylea/Avastin trial fails (bear-case 2).** We see this outcome as unlikely given the strength of the Phase 2b data, and Ophthotech has stated that the company would defer submission of regulatory applications under this scenario. FDA and EMA would likely request additional studies before granting any marketing authorization.

- **Only one Lucentis trial works, but the Eylea/Avastin trial works (bear-case 3).** We don't see a high likelihood of this outcome. However, under this scenario Ophthotech has stated that it would still submit marketing applications to the FDA and EMA. Under this path of events, the FDA and EMA could request additional studies before granting any marketing authorization. However, we see a conditional approval here as the more likely route followed by some confirmatory work for Lucentis to garner full approval.

- **All three Phase 3 trials fail (extreme bear case).** We see this outcome as highly unlikely, though would likely place the future development of Fovista in significant jeopardy.

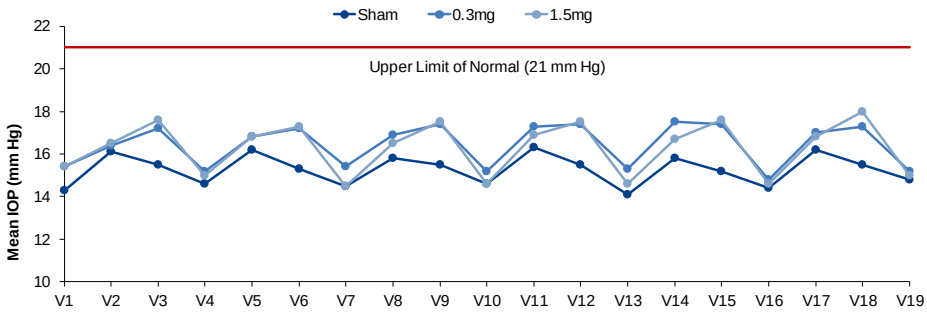
Potential FDA/EMA Label Issues Around Waiting Period Between Injections Seem Minor. There is some risk that a future label could stipulate a ~30-minute (or different) waiting period between injecting the anti-VEGF and injecting Fovista, as this is the protocol in the Phase 3 trials. We do not see this as a major issue as our discussions with retinal physicians suggest that the retinal specialist community (~2,000 in the US) tends to approach care more empirically than other specialties, meaning language in FDA labels may not always dictate individual practice patterns. In fact, we understand that the advent of Avastin's substantial off-label use in wAMD has its roots in this empirical disposition to retinal care. Regardless, should the label specify an injection time gap, Ophthotech would conduct a post-marketing trial to confirm that immediate injection of Fovista after the anti-VEGF is safe, as well as contemplate a study co-formulating Fovista with an anti-VEGF agent.

Fovista Adoption

The majority of our interactions with retinal specialists indicated that with careful technique and patient selection, they do not see a problem with two separate injections. A minority of retinal specialists we consulted questioned the feasibility of a second injection given intraocular pressure monitoring requirements that could delay patient throughput in the clinic. However, Macugen (first anti-VEGF approved for wAMD, but used infrequently today given better results with Lucentis/Eylea/Avastin) contains 90 µL of fluid which is comparable to anti-VEGF (50 µL) + Fovista (50 µL). Additionally, the Macugen dose is delivered in one injection, while the ~11% higher 100 µL for anti-VEGF + Fovista is split, with a 30-minute gap between injections.

Exhibit 19

Mean Peak Eye Pressures in Fovista Phase 2b Well Below Upper Limit of Normal



Key to Visit Numbers

V1 Day 0 (Pre-Injection)	V6 Week 4 (30´ After 2nd Inj.)	V11 Week 12 (30´ After 1st Inj.)	V16 Week 20 (Pre-injection)
V2 Day 0 (30´ After 1st Inj.)	V7 Week 8 (Preinjection)	V12 Week 12 (30´ After 2nd Inj.)	V17 Week 20 (30´ After 1st Inj.)
V3 Day 0 (30´ After 2nd Inj.)	V8 Week 8 (30´ After 1st Inj.)	V13 Week 16 (Pre-injection)	V18 Week 20 (30´ After 2nd Inj.)
V4 Week 4 (Pre-Injection)	V9 Week 8 (30´ After 2nd Inj.)	V14 Week 16 (30´ After 1st Inj.)	V19 Week 24
V5 Week 4 (30´ After 1st Inj.)	V10 Week 12 (Pre-injection)	V15 Week 16 (30´ After 2nd Inj.)	

Sources: Ophthotech Reports, Oppenheimer Research; emedicine.medscape.com.

Further, data from Ophthotech's Phase 2b trial demonstrate equilibration of intraocular pressures 30 minutes after the second injection and even peak pressures were well below the upper limit of normal of 21 mm Hg (Exhibit 19). That said, Exhibit 19 reports mean pressures, and Ophthotech apparently has not disclosed what percent of patients in the study may have exceeded 21 mm Hg. However, we are fairly comfortable with this data as a mean peak of ~18 mm Hg suggests relatively few patients may have transiently exceeded 21 mg Hg.

The co-formulation debate. The potential for a co-formulated VEGF/PDGF inhibitor product (e.g., as being developed by Regeneron and Allergan) has created an understandable debate about the Fovista tail (i.e., sales post 2020 when co-formulated products could launch) given Fovista's requirement for a second injection. We think a few points are relevant here.

1. **The co-formulation risk has already been absorbed into our long-term share assumptions for Eylea.** We see Fovista share falling to ~5% by 2020 given Regeneron's potential PDGF/VEGF co-formulation launch. Based on this, we see Fovista's blended share across all anti-VEGF's peaking at 24% in 2020 and then falling to 20% by 2024 as Regeneron captures share with its PDGF/VEGF co-formulation.

2. **Not co-formulating Fovista might be a plus for Avastin patients.** The availability of a non-co-formulated PDGF inhibitor is important despite a traditionally price-sensitive Avastin patient pool. We see a new value proposition potentially emerging where Fovista could offer Avastin patients the potential to achieve ~60% better vision (per Fovista Phase 2b data) than current care, and with a lower co-pay (we assume $1,450 per dose for Fovista) than for Eylea ($1850) or Lucentis ($1950). We see this as an interesting dynamic in the wAMD market that suggests Avastin share could *increase* with the Fovista launch. However, we have to wait for market data to validate this hypothesis and/or the magnitude/rate of any potential share shift to Avastin.

3. **With Novartis, Ophthotech management has advanced a long-term strategy that recognizes a need to remain competitive on co-formulation should the market move in that direction in ~5+ years when Regeneron launches.** While the details are understandably fairly unclear on how marketing of a Fovista-Lucentis co-formulation in the US may play out (i.e., Novartis markets with royalty to Ophthotech, vice versa, or some co-promote profit split), our overall impression is that the economics would be +/- comparable to what Ophthotech would have generated with marketing Fovista independently in the US.

Payor hurdles seem manageable, but launch will clarify. Despite an overall cost of therapy per injection series approaching $3,000-$3,500, provided the Phase 3 data generate the level of benefit seen in the Phase 2b, we believe payors would be hard-pressed not to cover Fovista. For newly diagnosed wAMD patients, some payors may enforce a step-edit requiring demonstrating ineffective response to an anti-VEGF before reimbursing for Fovista (notwithstanding that the Fovista label will have been based on trials in newly diagnosed wAMD patients). This seems like a minor issue to us, however, because the incident pool of wAMD patients starting anti-VEGF therapy is just ~10% of the prevalent anti-VEGF pool, and eventually ~25% of the incident patients would flow to the "immediate additional efficacy required" bucket.

Co-pays. Based on our physician checks, for the ~25% of anti-VEGF patients identified by retinal specialists where immediate additional efficacy is required and desired by the patient, we do not see the additional patient co-pay for Fovista as a major barrier to adoption among current Eylea/Lucentis patients. That said, in a bear case where the Phase 3 data suggest a more modest benefit even in the context of a Fovista approval, the co-pay hurdle could prove more substantial.

Some Minor Unresolved Issues Around Phase 3 Design

Treatment frequency details in second year still a moving target. Ophthotech will submit marketing applications based on results from the 12-month primary endpoint across all three Phase 3 trials. However, the trials will continue into a second year during the regulatory review process. In all three trials, patients will be treated every four weeks during the first year, apart from the Eylea patients who will receive monthly injections for three months (Q4W) and then every other month (Q8W). In the second year, current plans call for treatment every eight weeks (patients still assessed monthly), except for Avastin patients who will continue on Q4W. However, under certain circumstances suggesting visual decline (> 5 decrease in ETDRS or negative findings on fluorescein angiography or SD-OC), treatment at the alternate month visit is permitted. Any changes to the treatment frequency for year two will be settled before any patients reach the second year of treatment. While data for year two will not contribute to the primary endpoint, the FDA and/or EMA may request and consider safety data for months 12-24 in making a determination on approvability. **Overall, however, we see the details on dosing frequency in year two of the Phase 3 program as less of an issue for approvability than for commercial uptake in demonstrating the ability to treat and extend consistent with the treatment paradigm for the anti-VEGF drugs.**

CHMP concerns around combining Fovista with Avastin or Eylea. The CHMP has advised Ophthotech to consider toxicity studies for previously untested combinations of Fovista + Avastin and Fovista + Eylea before commencing Phase 3 studies. We would expect Ophthotech's pre-clinical work testing these combinations to satisfy the CHMP requests. Additionally, Ophthotech has indicated that sites have already been activated, so we do not anticipate any problems here.

Fovista Competition

The competitive landscape for wet AMD is fairly crowded with multiple players and a range of therapeutic strategies. However, there are a limited number of players specifically developing anti-PDGF therapies, anti-VEGF/anti-PDGF co-formulations, or dual anti-VEGF/anti-PDGF drugs (see Exhibit 20). We see the greatest potential long-term threats to Fovista from the co-formulated therapies, but they are two to three years behind Fovista, giving Ophthotech a meaningful first-mover advantage.

Regeneron is developing an anti-PDGF monoclonal antibody (REGN-2176) co-formulated with Eylea, meaning patients can receive both the anti-VEGF and the anti-PDGF via a single injection (see pp. 13-14 for a detailed discussion on the co-formulation debate). As an antibody, REGN-2176 is likely less potent on PDGF than Eylea is on VEGF, given Eylea's ~ 0.5 pM dissociation constant for VEGF165 and VEGF121, which seems to be beyond the affinity range of even very high-affinity antibodies (~10^{-11} - 10^{-12} M) [5]. Additionally, it is unclear whether REGN-2176's affinity for PDGF exceeds Fovista's ~100 pM (~10^{-10} M) affinity, which approaches the upper range of affinities (low nM) seen with high affinity monoclonal antibodies, though still below very high affinity antibodies. Regeneron is currently enrolling patients in Phase 1 to determine the safety and appropriate dosing regimen of REGN-2176, with an estimated completion date of February 2015 (per clinicaltrials.gov).

Allergan is planning to start clinical trials for AGN151200 (dual anti-VEGF/anti-PDGF DARPin) in 2014. While we do not expect any changes in the AGN151200 development plan under Allergan, a potential merger with Valeant could lead to a re-evaluation of the pipeline and the level of investment in the DARPin program.

Exhibit 20

PDGF Inhibitor Competitive Landscape

Company	Drug	Class	Route	Stage	Target	Comments
Bayer/ Regeneron	PDGFR-B antibody for co-formulation with Eylea, REGN-2176	mAB	Injection	Phase 1	PDGF	Estimated Primary Completion Date for Phase 1 is February 2015
Neurotech	NT-506	PDGF antagonist	ECT implants secreting PDGF-antagonists	Pre-clinical	PDGF	Could be compatible with Neurotech's anti-VEGF implants (NT-503) already in clinic
Allergan, Molecular Partners	MP0260 / AGN-151200	DARPin (dual VEGF-A/PDGF-B) co-formulated	Injection	Pre-clinical	PDGF VEGF	Phase 1 to start in 2014
Ohr Pharmaceuticals	Squalamine Lactate	Inhibitor of calmodulin, preventing downstream signaling of VEGF, PDGF, and bFGF	Eye drops	Phase 2	PDGF VEGF bFGF	See text (page 16)
Santen	DE-120	dual inhibitor of VEGF and PDGF	Injection	Phase 1/2a started January 2014	PDGF VEGF	Estimated Primary Completion Date June 2016
Xcovery Vision	X-82	Small molecule inhibitor of VEGF, PDGF, and bFGF	Oral tyrosine kinase inhibitor (X-82)	Phase 1/2	PDGF VEGF	Estimated Primary Completion date June 2014
GlaxoSmithKline	Pazopanib	Multikinase tyrosine inhibitor (PDGFR, VEGFR, c-KIT)	Eye drops	Phase 2b	PDGFR VEGFR c-KIT	Phase 2a terminated in 2012
Lpath / Pfizer	Sonepcizumab	Monotherapy or adjuncitve therapy to anti-VEGF	Injection	Phase 2a (includes previous anti-VEGF treated pts)	Sphingosine 1 phosphate	Estimated Primary Completion date November 2014

Sources: clinicaltrials.gov, Oppenheimer Research.

[5] http://www.abcam.com/index.html?pageconfig=resource&rid=15749&source=pagetrap.

Neurotech appears to be developing a combination therapy for wet AMD based on cellular implants that secrete ophthalmic drugs. However, the company's anti-PDGF implant (NT-506) is preclinical with unclear timelines for advancement into human studies. Eventually, NT-506 could be compatible with Neurotech's anti-VEGF implants (NT-503) already in the clinic or anti-VEGF injections.

Some other mechanisms being explored in wAMD outside of anti-VEGF/PDGF include multi-kinase inhibition (i.e., GSK's pazopanib, Santen's DE-120, and Xcovery's X-82) or downstream blockade of the VEGF/PDGF signaling pathway (Ohr's squalamine eye drops inhibit calmodulin signaling; see comments below).

A word on Ohr's recent data[6]. Ohr recently presented interim data from its ongoing Phase 2 wAMD trial of squalamine eye drops in combination with Lucentis showing a ~65% benefit in visual acuity vs. Lucentis monotherapy, which missed statistical significance (p-value = 0.18) possibly given low power (N = 62). However, the visual acuity gains at week 38 appear on par with Ophthotech's data at a shorter 24 weeks. The market appeared to focus on Ohr's having missed the primary endpoint (failed to reduce the mean number of Lucentis injections vs. Lucentis alone), but at least initially the visual acuity looked fairly good, which seems like the more relevant data point to us. Full data are expected in 2H14 and, among other details, we are interested in seeing the degree of compliance on the drops. On one hand, the possibility of replacing a PDGF injection ~4x yearly (our model assumption for Fovista) with BID eye drops seems appealing, but we have questions about real-world compliance, particularly in an older population likely on multiple medications. That said, we have not yet performed detailed diligence with retinal specialists on this issue. However, we suspect that the opportunity to retain ~100% compliance on an infrequent injection schedule that includes anti-PDGF therapy could be preferable to twice-daily eye drops in a substantial number of patients. **Regardless, we believe our ~25% peak share assumption for Fovista across the anti-VEGFs embeds enough conservatism should Ohr eventually take some share of the combination market.**

Fovista Pipeline

A range of non-pivotal trials for Fovista with data expected in 2015 and 2016 could broaden Fovista's long-term commercial prospects and provide a step-up in the adoption curve with an expected initial approval (~2017) in combination with anti-VEGF therapy. <u>However, pending proof-of-concept, we do not include any value in our model for these additional Fovista applications and/or indications</u>.

<u>TRIAL 1:</u> Anti-Fibrosis Trial in Wet AMD. Ophthotech is planning to initiate in 2014 a Phase 2 trial (N = ~100 wAMD patients) to explore whether Fovista can reduce or slow the formation of subretinal fibrosis. Initial data are expected in late 2015 or early 2016. The study is supported by a variety of pre-clinical and clinical evidence pointing to negative outcomes with subretinal fibrosis and PDGF inhibition's potential role in counteracting fibrosis (see Exhibit 21).

<u>TRIAL 2:</u> Von Hippel-Lindau disease. The National Eye Institute is planning to initiate a clinical trial in 2014 testing Fovista in ~20 Von Hippel-Lindau (VHL) patients with retinal capillary hemangiomas (RCH). VHL is a rare (N ~ 5000 in the US) inherited disease characterized by multiple benign and malignant tumors and cysts in the eye and other organs and caused by a deficiency in a protein called pVHL. The disease leads to ocular tumors consisting of blood cells called retinal capillary hemangiomas (RCH), which can cause retinal leakage and vision loss. PDGF has been shown to be elevated in cells with deficient pVHL, so Fovista + an anti-VEGF therapy may benefit patients with RCH.

<u>TRIAL 3:</u> Proliferative vitreoretinopathy. Ophthotech is planning to initiate in 2015 a clinical trial enrolling ~20 patients with PVR to test Fovista when combined with surgery (standard of care). We estimate that there are approximately 5,000 to 10,000 new cases of PVR in the United States each year. Proliferative vitreoretinopathy (PVR) is a complication occurring in ~5-10% of retinal detachments, leading to retinal scarring. With recurrence, poor visual outcome is likely and often untreatable. Local concentrations of

Exhibit 21

Evidence Supporting Fovista's Potential to Address Fibrosis in anti-VEGF treated wAMD patients

Subretinal fibrosis is considered a reliable biomarker for predicting poor final visual outcomes in late stage wAMD
45% of wet AMD patients developed subretinal fibrosis after two years of treatment with an anti-VEGF drug †
Anti-VEGF treatment may trigger subretinal fibrosis as early as 3 months on therapy, with severity of fibrosis associated with more severe vision loss *
PDGF is a mediator of fibrosis in multiple pre-clinical models of organ fibrosis and retinal scarring
Fovista monotherapy was shown to be anti-fibrotic in a preclinical model of retinal scarring and fibrosis
In patients with visual loss ? 0 letters, subretinal fibrosis was seen in up to 69% of Lucentis patients vs. 30% of Fovista (1.5mg) + Lucentis patients in the Phase 2b ‡

Sources: * *Am J Ophthalmol* 2013;156:116-124.

† Retrospective analysis of the CATT trial (New England Journal of Medicine 2011. 364 (20): 1897–1908).

‡ Retrospective retinal imaging

[6] Recall that squalamine administration by intravitreal injection proved unsuccessful in animal models (see *Ophthalmol Clin N Am* 19 (2006) 381–391). Genaera had formerly been developing squalamine systemically for wAMD with some good Phase 1/2 data, but abandoned the product (*Ophthalmol Clin N Am* 19 (2006) 381–391).

PDGF may be elevated in patients suffering from PVR, and Fovista strongly inhibited retinal scarring in an animal model of PVR. Fovista combined with surgery could prove beneficial in PVR patients. There are no FDA-approved drugs for PVR.

TRIAL 4: Reduction of Treatment Burden: Ophthotech plans to initiate in 2014 a Phase 2 trial enrolling ~30 wAMD patients to assess whether Fovista + anti-VEGF drugs can reduce the number and frequency of intravitreal anti-VEGF injections needed to effectively treat wet AMD. Initial data are expected in 2015, which, if positive, could lead to further exploration of the treatment burden reduction hypothesis in a larger study (N ~ 100). Rationale for this study is based on retrospective analyses from the Phase 2b wAMD trial suggesting Fovista + Lucentis drove larger reductions in the size of the neovascular complex vs. Lucentis monotherapy. We view the hypothesis surrounding this trial as fairly speculative.

TRIAL 5: Anti-VEGF failures/non-responders. Ophthotech plans to initiate in 2015 a Phase 2 trial in ~30 wet AMD patients to test whether Fovista + an anti-VEGF may provide clinical benefit in patients previously treated with anti-VEGF therapy who do not achieve significant visual gain or experience visual decline (~20% of newly diagnosed wAMD patients). Data are anticipated in early 2015. Successful data could trigger a larger (N ~ 100) trial to commence in 2015.

We await details from Ophthotech (possibly in 2H14) on greater specifics for the above studies (i.e., randomized or not, control arm details, etc.).

Fovista Basics

Fovista is a DNA aptamer conjugated to 40 kDa PEG (i.e., pegylated, which provides extended half-life in vivo). Fovista binds to PDGF-AB or PDGF-BB with a K_d of approximately 100 pM and inhibits the functions of PDGF-B both in vitro and in vivo. DNA aptamers are short strands of oligonucleotides that usually have high binding affinities for various targets, though perhaps with somewhat lower affinity than antibodies. Aptamers have several advantages over antibodies, including scalability, fast and inexpensive production, low toxicity, and relatively small size. Fovista (formerly E10030) was discovered at NeXstar Pharmaceuticals (see Green, L.S., et al. (1996) Biochemistry 35: 14413 and US Patents 6,207,816; 5,731,144; 5,731,424; and 6,124,449).

Mechanism of Action. Fovista works synergistically with VEGF antagonists by binding to platelet-derived growth factor (PDGF) and inhibiting recruitment of pericytes. Fovista strips away pericytes, exposing abnormal vasculature to anti-VEGF agents. In pre-clinical models, Fovista promoted neovascular regression when co-administered with a VEGF antagonist. These results were replicated in Ophthotech's Phase 1 and 2 studies when patients treated with combined Fovista and Lucentis demonstrated evidence of neovascular regression, whereas patients in the PIER, ANCHOR, and MARINA trials of Lucentis monotherapy achieved gains in visual acuity without concurrent neovascular regression. In the Phase 1 study, 91% of combination therapy patients had evidence of neovascular regression on fluorescein angiogram compared to 16% on monotherapy. In their Phase 2b study, patients receiving combination therapy achieved greater reductions in choroidal neovascularization disc size and resolution of subretinal hyper-reflective material relative to monotherapy patients.

Zimura – Potential in Wet and Dry AMD

Ophthotech has completed two clinical studies for Zimura in **1)** geographic atrophy and **2)** wet AMD. **We have yet to see proof-of-concept for Zimura in either indication, so we are not currently including Zimura in our model.** That said, there are no FDA- or EMA-approved therapies for dry AMD, so future positive clinical trial results could cause us to become more positive on Zimura's value.

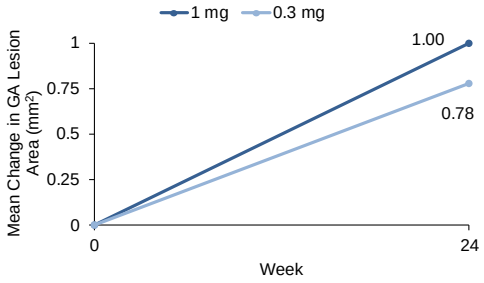
Geographic atrophy trial. Ophthotech completed an uncontrolled, open-label Phase 1/2a study of Zimura monotherapy in geographic atrophy. The 47-patient trial was not powered to detect differences in dose groups (1:1 randomized to 0.3 mg or 1.0 mg). Five injections were administered over 36 weeks (day 0, week 4, week 8, week 24 and week 36). Over the first 24 weeks of the trial, the mean growth from baseline in the geographic atrophy lesion area was 1.00 mm^2 (N = 24 at 0.3 mg) vs. 0.78 mm^2 (N = 23 at 1.0 mg), a favorable but non-significant dosing trend. Safety was unremarkable. **While these**

results suggest a potential effect of dose, the data are hard to interpret without a control arm.

Wet AMD trial. Ophthotech completed an uncontrolled, open-label Phase 2a study of Zimura in 60 wAMD subjects. A subgroup of 43 anti-VEGF naïve patients received six injections of Zimura at doses of 0.3 mg, 1.0 mg or 2.0 mg + Lucentis. At week 24, there was an improvement in mean visual acuity from baseline of 13.6 letters for 13 patients receiving 0.3 mg, 11.7 letters for 15 pts treated with 1.0 mg, and 15.3 letters for 15 patients receiving 2.0 mg of Zimura. In this subgroup, 22 patients (51%) gained at least three lines of vision, consisting of six patients (46%) in the 0.3 mg dose group, seven patients (47%) in the 1.0 mg dose group and nine patients (60%) in the 2.0 mg dose group. Combining Zimura with an anti-VEGF was generally well tolerated.

Exhibit 22

Some Signs of Zimura Efficacy in Uncontrolled 2-Dose Trial



Sources: Ophthotech Reports, Oppenheimer Research.

Zimura Clinical Development

Geographic atrophy. Ophthotech is preparing to initiate a randomized, controlled Phase 2/3 trial of Zimura monotherapy in dry AMD by late 2014 or early 2015. Interim data are anticipated in 2016. The study is expected to enroll ~300 patients at ~50 US and EU sites, and patients will be randomized to monthly Zimura or sham injection for up to 18 months. The expected primary endpoint is the difference in the mean change in geographic atrophy lesion area vs. baseline.

Anti-VEGF resistant wet AMD patients. The company is also in the planning stages of a Phase 2 trial in wet AMD patients believed to have complement-mediated inflammation. The study is expected to start in 2015 with initial data in 2016. ~100 patients will be randomized to Zimura + Fovista + anti-VEGF and Fovista + anti-VEGF, to explore the potential of Zimura in addressing impacting complement mediated inflammation.

Zimura Competition

A number of companies are developing therapies targeting the complement system that are at a more advanced stage of development than Zimura, but success has not been widespread (Exhibit 23). The major contenders with positive data, as we see them, are Roche's Lampalizumab (targets complement Factor D target) and Novartis's LFG316 (also targets C5). **However, the failure of Alexion's Phase 2/3 trial of Eculizumab in dry AMD (also targets C5 like Zimura) suggests a fair amount of risk around the C5 approach despite some positive trends for Zimura seen in its uncontrolled geographic atrophy trial.**

Roche's Lampalizumab. This agent was the first complement inhibitor to demonstrate efficacy in geographic atrophy and targets Factor D not C5. The Phase 2 MAHALO study (N = 129) met its primary efficacy endpoint with patients achieving a 20.4% reduction in geographic atrophy progression vs. sham injection. A Phase 2 18-month extension study is currently evaluating long-term safety and tolerability of repeated intravitreal administration of lampalizumab. No dose-limiting toxicities or drug-related adverse events were observed in Phase 1a.

Alexion's Eculizumab. Eculizumab did not appear to provide clinical benefit in dry AMD (geographic atrophy and presence of drusden) despite targeting C5 intravenously,

inconsistent with the trend toward geographic atrophy reduction seen in Zimura. While the lack of a C5 inhibition benefit should be a concern to Ophthotech, there are major differences between Eculizumab and Zimura's study populations (Zimura specifically targets geographic atrophy), mode of administration, and target specificity (mAb vs. aptamer). It is possible that Zimura has higher C5 target-affinity, preventing the activation of alternative C5 cleavage pathways missed by Eculizumab.

Novartis. Additionally, although unsuccessful in wet AMD, Novartis's Alcon began investigation of POT-4 for dry AMD using an extended-release (six-month) injectable gel targeting C3 but has not entered clinical testing in dry AMD. This delivery system could eliminate the burden of monthly injections and potentially offer a more commercially attractive candidate than either Lampalizumab or Zimura were POT-4 to demonstrate efficacy in dry AMD.

Exhibit 23

Dry AMD & Geographic Atrophy Competitive Landscape

Company	Drug	Class	Route	Stage	Target	Comments
Acucela	ACU-4429 (emixustat)	Small molecule	Oral	Phase 2b/3	Retinal pigment epithelium 65	Phase 2 completed June 2012; Phase 1 PK study ongoing
Advanced Cell Technology	MA09-hRPE	Stem cell	Sub-retinal transplantation	Phase 1/2	Embryonic stem cells to replace damaged RPE cells	Data 2H14
Alexion	Eculizumab	Humanized IgG antibody	Intravenous	Phase 2	C5	Failed to demonstrate clinical benefit in dry AMD and geographic atrophy
Alimera Sciences	Iluvien (Fluocinolone acetonide)	Corticosteroid	Intravitreal implant	Phase 2	Fluocinolone suppresses VEGF	Data YE14
Allergan	Alphagan	Brimonidine tartrate	Intravitreal Implant	Phase 2	a2 adrenergic receptor	Data 2018
GSK	GSK933776	Anti-amyloid B antibody	Intravenous	Phase 2	Beta-amyloid	1H16
iScience, Johnson & Johnson	CNTO2476	Stem cell	Catheter implant	Phase 1/2	Human Umbilical Tissue to replace damaged RPE cells	Data 1H15 (but study on clincal hold)
MacuClear	MC-1101	Anti-hypertensive	Eye drop	Phase 2/3	Prevent Bruch membrane rupture by increasing choroidal blood flow	Data 1H16
Macusight/ Santen	Sirolimus	Rapamycin	Subconjunctival injection (3 month)	Phase 1/2	mTOR	Failed to demonstrate benefit
Novartis (Alcon)	CLG561	Unspecified	Intravitreal Injection	Phase 1	Unspecified	Data 2H14
Novartis, MorphoSys	LFG316	Fully human antibody	Intravitreal Injection	Phase 2	C5	Data 2018
Potentia, Novartis (Alcon), Apellis	POT-4 (APL-1)	Compastatin derivative	Sustained release (6 months) gel injection	Phase 2	C3	Failed in wAMD in Phase 1 - majority of patients experienced no improvement in visual acuity
Roche (Genentech)	Lampalizumab (FCFD4514S, RG7417)	Humanized monoclonal antibody fragment	Intravitreal Injection	Phase 2	Complement Factor D	20.4% reduction in the area of geographic atrophy (MAHALO trial)

Sources: clinicaltrials.gov, Oppenheimer Research.

Zimura Basics

Zimura is an RNA aptamer conjugated to 40 kDa PEG. Aptamers are short strands of oligonucleotides, usually showing robust binding affinities for various targets. Nucleic acid aptamers bind numerous targets with high specificity and affinities similar to antibodies. The advantages of using aptamers are scalability, fast and inexpensive production, low toxicity, and relatively small size.

Mechanism. Zimura, a pegylated RNA aptamer licensed from Archemix, is an inhibitor of complement factor C5 that is associated with complement-mediated inflammation and cell damage believed to be involved in dry and certain forms of wet AMD, as well as possibly anti-VEGF resistance. Inhibiting C5 may prevent the formation of key terminal protein fragments (C5a and C5b) responsible for the buildup of drusen (protein deposits) in the retina which can over time lead to VEGF and PDGF activation.

Valuation

Exhibit 24

DCF Valuation

Time of Valuation	Jun-14
WACC	**12.5%**
Intermediate CF Growth (2025 - 2030)	2.0%
Terminal FCF Growth	0.0%
Discounted FCF (2014 - 2030) $MM	$2,259
Terminal FCF Value $MM	$405
Total PV FCF $MM	$2,663
Cash $MM 2Q14	$422
Debt $MM	$0
Equity Value $MM	**$3,086**
Shares Oustanding (MM) 2Q14	32.4
DCF Value / Share	**$95**

Source: Oppenheimer Research Estimates.

Valuation Method: We value Ophthotech using a discounted cash flow (DCF) analysis with a WACC of 12.5% and a 0% terminal growth rate post 2030. Since we model the cash cost of options, we use the basic share count to avoid double-counting.

Discount Rate: Our valuation framework utilizes a 12.5% discount rate for pre-commercial stage companies that have achieved clear Phase 2 proof-of-concept.

Terminal Growth Rate: We explicitly model cash flows to 2024. From 2025 to 2029, we grow cash flows at 2%. After 2029, we assume a terminal growth rate of 0% given expiration of market exclusivity and potential generic Fovista entrants, yielding a terminal value of ~$405 million. Fovista appears eligible for 13 years of market exclusivity given an assumed 2017 launch, the expiration of the MOU patent[7] covering the treatment of wet AMD with Fovista + an anti-VEGF in 2024, and addition of the maximal five years of Hatch-Waxman patent extension.

Exhibit 25

Catalyst Calendar

Drug	Type	Event	Timing
Fovista	Clinical Data	Von Hippel-Lindau Disease with NEI, Phase 2 Readout	2015
Fovista	Clinical Data	Anti-VEGF Treatment Failures (+ anti-VEGF) Phase 2 Initial Readout	2015
Fovista	Clinical Data	Reduction of Treatment Burden (+ anti-VEGF) Phase 2 Initial Readout	2015
Fovista	Clinical Data	Anti-Fibrosis (+ anti-VEGF) Phase 2 Initial Readout	Late 2015
Fovista	Clinical Data	Fovista + Lucentis Phase 3 Readout (Trial 1)	Mid-2016
Fovista	Clinical Data	Fovista + Lucentis Phase 3 Readout (Trial 2)	Mid-2016
Fovista	Clinical Data	Fovista + Avastin / Eylea Phase 3 Readout	Mid-2016
Zimura	Clinical Data	Dry AMD Phase 2/3 Interim Readout	2016
Fovista	Clinical Data	Proliferative Vitreoretinopathy Phase 2 Readout	2016
Zimura	Clinical Data	Wet AMD Anti-VEGF Resistant (+ anti-VEGF, + Fovista) Phase 2 Readout	2016
Fovista	Product Advancement	Submit Applications for Marketing Approval in US and EU	Late 2016

Sources: Ophthotech Presentations, Oppenheimer Research.

[7] The last to expire issued COM patents for Fovista are 2017 (US) and 2018 (EU and Japan).

Wet AMD Model Assumptions

wAMD patient population growth. The number of Americans with wet AMD is projected to grow from 1.7 million in 2010 to 3 million in 2020, owing to population growth, longer survival and a large population of Americans shifting into the older age categories at greatest risk for AMD.

Addressable wAMD population. We assume 27% of wAMD patients are treated with anti-VEGF therapy, consistent with the known wAMD prevalence and our calculations on anti-VEGF treated patients in the US.

Anti-VEGF Share:

1) **Avastin.** We assume 25% peak share of Avastin patients, which reflects a balance between cost sensitivities driving Avastin use and the potential for some share shift to Avastin. Our argument is that Avastin + Fovista could drive ~60% better visual acuity at ~45% of the cost of Eylea/Lucentis + Fovista (i.e., ~$3300-3450).

2) **Eylea.** We assume peak share of 25% in 2020. In 2021+, we ramp down Fovista share of Eylea-treated patients to 5% by 2024 in view of the potential approval of Regeneron's PDGF beta antibody for co-administration with Eylea in ~5 years (their VEGF/PDGF combination product is currently in Phase 1).

3) **Lucentis.** We assume peak share of 35%. While Ophthotech owns Fovista in the US, knowledge of Ophthotech and Novartis working together on a potential co-formulation suggests retinal specialists may be slightly more inclined to develop experience with Fovista + Lucentis than either + Eylea or + Avastin.

4) **Ramp.** We assume a ramp slightly more conservative than the two-year ramp for Eylea (significant sales first in 2012, 26% market share in 2013).

Number of injections per year: Four per eye on average. We see this assumption as conservative relative to Lucentis ~9 injections per year and Eylea's ~6-7 injections per year.

Average number of wAMD eyes per subject: Approximately ~40% of wAMD patient have bilateral disease, so we incorporate this assumption into our model (see *Graefes Arch Clin Exp Ophthalmol.* 2011 Apr;249(4):521-7).

Pricing: $1450 per injection. Lucentis' WAC is ~$2000 per injection and Eylea's is $1850. We are therefore assuming a ~27% discount to Lucentis and a ~22% discount to Eylea. Some investors have approached the pricing question by calculating the relative visual acuity benefit Fovista + Lucentis delivered over Lucentis in Phase 2b, or 62%. In other words, each additional letter of vision gained should be worth approximately ~$300, or ~$1200 per injection, based on the ~4 letter benefit seen in Ophthotech's Phase 2b. We believe management will pursue a somewhat more aggressive strategy to the eventual pricing question, and we are comfortable with our $1450 assumption.

Exhibit 26

Fovista Market Model (US and EU)

Fovista wAMD Market Model	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
US Fovista (patients, $ in millions)											
US AMD Prevalence	15	16	18	19	21	23	25	28	30	33	36
% with wAMD	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
US wAMD Prevalence	1.75	1.91	2.08	2.27	2.48	2.70	2.95	3.22	3.51	3.83	4.18
US wAMD Incidence		0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3
% with wAMD treated with VEGF	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%
Treated with VEGF inhibitor	0.48	0.52	0.57	0.62	0.68	0.74	0.80	0.88	0.96	1.04	1.14
Avastin Patients	0.24	0.26	0.28	0.31	0.34	0.37	0.40	0.44	0.48	0.52	0.57
% share of wAMD market	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Eylea Patients	0.12	0.13	0.15	0.16	0.18	0.20	0.21	0.23	0.25	0.28	0.30
% share of wAMD market	25%	26%	26%	27%	27%	27%	27%	27%	27%	27%	27%
Lucentis Patients	0.12	0.13	0.14	0.15	0.16	0.17	0.19	0.21	0.22	0.25	0.27
% share of wAMD market	25%	25%	24%	24%	24%	24%	24%	24%	24%	24%	24%
Fovista Add-on to Avastin				0.02	0.05	0.07	0.10	0.11	0.12	0.13	0.14
Fovista % share of Avastin				5%	15%	20%	25%	25%	25%	25%	25%
Fovista Add-on to Eylea				0.01	0.03	0.05	0.05	0.05	0.04	0.03	0.02
Fovista % share of Eylea				5%	15%	25%	25%	20%	15%	10%	5%
Fovista Add-on to Lucentis				0.01	0.02	0.04	0.06	0.07	0.08	0.09	0.09
Fovista % share of Lucentis				5%	15%	25%	30%	35%	35%	35%	35%
Blended Fovista % share of VEGFs				5%	15%	23%	26%	26%	25%	23%	22%
Total US Patients on Fovista				**0.03**	**0.10**	**0.17**	**0.21**	**0.23**	**0.24**	**0.24**	**0.25**
Fovista Price per Injection				$1,450	$1,450	$1,450	$1,450	$1,450	$1,450	$1,450	$1,450
Annual Price Increase					0%	0%	0%	0%	0%	0%	0%
Gross-to-net adjustment				10%	10%	10%	10%	10%	10%	10%	10%
Net Fovista Price per injection				$1,305	$1,305	$1,305	$1,305	$1,305	$1,305	$1,305	$1,305
Fovista average vials / eye / patient / year				2.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
wAMD % bilateral				38%	38%	38%	38%	38%	38%	38%	38%
Fovista average vials / patient / year				2.8	5.5	5.5	5.5	5.5	5.5	5.5	5.5
Fovista US Revenue				**$111**	**$729**	**$1,193**	**$1,514**	**$1,642**	**$1,700**	**$1,755**	**$1,806**
EU Fovista (patients, $ in millions)											
EU AMD Prevalence	25	27	30	32	35	39	42	46	50	55	60
% with wAMD	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
EU wAMD Prevalence	2.92	3.18	3.47	3.79	4.13	4.51	4.92	5.36	5.85	6.38	6.96
EU wAMD Incidence		0.3	0.3	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.6
% with wAMD treated with VEGF	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%
Treated with VEGF inhibitor	0.46	0.50	0.55	0.60	0.65	0.71	0.77	0.84	0.92	1.01	1.10
Avastin Patients	0.13	0.14	0.15	0.17	0.18	0.20	0.22	0.24	0.26	0.28	0.31
% share of wAMD market	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%	27%
Eylea Patients	0.14	0.21	0.26	0.28	0.30	0.33	0.36	0.39	0.43	0.47	0.51
% share of wAMD market	30%	40%	45%	45%	45%	45%	45%	45%	45%	45%	45%
Lucentis Patients	0.20	0.17	0.16	0.17	0.19	0.21	0.22	0.25	0.27	0.29	0.32
% share of wAMD market	43%	33%	28%	28%	28%	28%	28%	28%	28%	28%	28%
Fovista Add-on to Avastin				0.00	0.01	0.01	0.01	0.01	0.02	0.02	0.02
Fovista % share of Avastin				1%	4%	5%	6%	6%	6%	6%	6%
Fovista Add-on to Eylea				0.01	0.02	0.04	0.05	0.04	0.03	0.02	0.01
Fovista % share of Eylea				3%	8%	13%	13%	10%	8%	5%	3%
Fovista Add-on to Lucentis				0.00	0.01	0.03	0.03	0.04	0.05	0.05	0.06
Fovista % share of Lucentis				3%	8%	13%	15%	18%	18%	18%	18%
Blended Fovista % share of VEGFs				2%	7%	11%	12%	12%	10%	9%	8%
Total EU Patients on Fovista				**0.01**	**0.04**	**0.08**	**0.09**	**0.10**	**0.10**	**0.09**	**0.09**
Fovista Price per Injection				$1,088	$1,077	$1,066	$1,055	$1,045	$1,034	$1,024	$1,014
Annual Price Decrease					-1%	-1%	-1%	-1%	-1%	-1%	-1%
Gross-to-net adjustment				10%	10%	10%	10%	10%	10%	10%	10%
Net Fovista Price per injection				$979	$969	$959	$950	$940	$931	$921	$912
Fovista average vials / eye / patient / year				2.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
wAMD % bilateral				38%	38%	38%	38%	38%	38%	38%	38%
Fovista average vials / patient / year				2.8	5.5	5.5	5.5	5.5	5.5	5.5	5.5
Fovista EU Sales				**$36**	**$234**	**$408**	**$485**	**$504**	**$489**	**$469**	**$442**
Novartis Royalty				*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
Effective Novartis Royalty*				*24%*	*24%*	*24%*	*23%*	*23%*	*23%*	*23%*	*22%*
EU Fovista Revenue to Ophthotech				**$9**	**$56**	**$96**	**$113**	**$116**	**$111**	**$105**	**$98**
WW Fovista Revenue to Ophthotech				**$120**	**$785**	**$1,289**	**$1,626**	**$1,758**	**$1,811**	**$1,861**	**$1,905**

* Ophthotech owes royalties to OSI, Nektar, Novo

Source: Oppenheimer Research Estimates.

Financial Model Assumptions

Revenue

US: Ophthotech owns full rights to Fovista and is expected to commercialize on its own. We model peak US Fovista of ~$1.8 billion in 2024.

EU: We model peak EU Fovista sales of ~$500 million in 2021 with peak royalty revenue to Ophthotech of ~$120 million.

Economics

Novartis: We amortize the net $180.25 million upfront ($19.75 million was paid to Nektar in 2Q14) over the life of the Fovista patent (2024 including five years Hatch-Waxman). We model and fully recognize the $130 million for completion of enrollment in the Fovista Phase 3 program in 2015. We assume a ~35% royalty on ex-US Fovista sales (guidance is "mid-thirties"). However, we understand that Ophthotech, not Novartis, will be responsible for fulfilling royalty obligations to OSI, Nektar and Novo A/S. Therefore the realized royalty from Novartis is assumed to be ~25%.

Third-party royalties: Ophthotech owes royalties on Fovista sales as follows: **1)** Novo A/S: low- to mid-single-digit percentage of worldwide sales of Fovista and we assume 4%, **2)** Nektar: tiered, low- to mid-single-digit percentage of worldwide sales of Fovista and we assume 4% ramping to ~6% by 2024, and **3)** OSI Pharma: low-single-digit percentage of worldwide sales of Fovista and we assume 3%.

Third-party milestone obligations: Additional aggregate milestone payments of $34 million spread across Novo, Nektar and OSI Pharma are assumed to be paid upon regulatory approval in 2016, although some milestones are due upon reaching unspecified commercial milestones. For instance, OSI is owed $12.0 million for approval of Fovista in the US and EU. For future milestones from Novartis, Nektar is owed a higher double-digit percentage of such revenues (recall Nektar received 9.875% of the $200 million Novartis upfront).

COGS: Fovista is a chemically synthesized pegylated DNA aptamer, not an antibody, so we expect COGS to more closely parallel small molecule costs, and we assume ~8% initially falling to ~6% by 2024 with the benefit of ramping volumes.

Operating Expenses

R&D: We see R&D ramping substantially in 2014-2016 with execution of the Fovista Phase 3 program and the initiation of a range of Phase 2 trials (see Catalyst Calendar, Exhibit 25). We assume all-in costs for the Fovista Phase 3 program of ~$150 million. Note that drug costs alone in Phase 3 to supply Lucentis and Eylea could approach ~$50 million (we estimate roughly 22,000 Lucentis injections and 4,000 Eylea injections).

SG&A: Ophthotech has stated an intention to commercialize Fovista independently in the US upon FDA approval. The company has assumed a sales and marketing force of <100 persons would be required, and we assume 75 persons (50 sales persons, 25 regional managers). We believe 50 sales reps should be sufficient to cover the approximate ~2,000 retinal specialists (cited by Ophthotech) in the US annually, as this would imply each rep would cover 40 accounts and could spend ~6-7 business days per year (i.e., one visit every other month) with each retinal specialist, which seems reasonable to us.

Financings: None modeled given the Novartis deal, which provides sufficient cash ($180 million net upfront received and $130 million expected in 2015 from for enrollment completion in Phase 3) through Fovista's expected US/EU launches in 2017. The royalty agreement with Novo A/S also provides an additional financing cushion ($41.7 million), which we do not model.

Risks to Price Target

Key risks to our price target include: 1) Universal failure across all Phase 3 trials or a range of split outcomes (see discussion above pp. 12-13) could jeopardize FDA and/or EMA approval, and/or require additional clinical work that delays cash flows and/or creates an unexpected financing gap. **2)** Although members of management have experience with launching back-of-the eye ophthalmic products (CEO David Guyer was CEO of EyeTech, which developed and launched Macugen), Ophthotech as an independent corporation has yet to establish a commercial infrastructure, distribution capabilities, or market any drug. **3)** Data only in 2016 could mean the stock retains a large discount to our estimated intrinsic valuation, creating risks around opportunity cost. **4)** Share gains among anti-VEGF treated patients could be weaker than projected if cost over Lucentis and Eylea and Avastin and the requirement for a second intravitreal injection emerge as greater headwinds than we currently believe. **5)** More rapid development and approval of competitive PDGF inhibitors, including products possibly co-formulated with existing anti-VEGF agents, could pressure Fovista share. **6)** Regulators could require additional non-clinical trials or require changes to the Phase 3 clinical program for Fovista (endpoints, enrollment criteria, selection of anti-VEGF drugs) that could delay progress of the Phase 3 program relative to the 2016 timeframe for top-line data, magnifying the opportunity cost.

Appendix I: Quick Background on AMD

Age-related macular degeneration (AMD) is the leading cause of adult-onset legal blindness in age > 50 cohort in the US. AMD is caused by degeneration of retinal cells in the area of the back of the eye known as the macula, which is needed to see fine detail. It is estimated that ~15 million people in the US suffer from some form of AMD. Prevalence of AMD is rising as the age >50 population increases. **There are two forms of AMD, dry (85-90% of cases) and wet.**

Dry AMD

Dry AMD is characterized by thinning and destruction of the retinal tissue in the macula resulting in gradual and irreversible vision loss. It is often accompanied by the appearance of yellow-white deposits, called drusen, that accumulate under the retina. As the number of drusen or their size increases, cells in the retina may become damaged, resulting in thinning and dysfunction of retinal tissue. Significant vision loss can result if dry AMD evolves into a more severe form, characterized by deep levels of macular tissue degeneration, known as geographic atrophy. However, the hallmark of dry AMD is the absence of new vascular growth into the retina. There are currently no FDA- or EMA-approved therapies for dry AMD.

Wet AMD

Ten to 15 percent of dry AMD cases progress to the more severe late-stage form of wet AMD. Wet AMD is characterized by the growth of abnormal new blood vessels (i.e., neovascularization) under the macular region of the retina, leading to fluid leakage, retinal distortion, scarring, and destruction of macular tissue. Wet AMD accounts for ~80-90% of all blindness associated with AMD, despite comprising only 10% of all AMD cases.

Role of PDGF in wet AMD. As neovascularization develops, rising levels of platelet-derived growth factor (PDGF) recruit pericytes that stabilize the neovascular complex (refer to Exhibit 3). PDGF may also contribute to the formation of subretinal fibrosis and retinal scarring that develops in the later stages of wet AMD. PDGF and pericyte coverage of neovasculature are believed to hinder the activity of anti-VEGF therapies, leading to visual deterioration even with optimal approved therapies.

Appendix II: Statistical Methods

We analyzed the probabilities of success in the Fovista Phase 3 trials using the Student's t-test (2-tailed) for difference between means, under the null hypothesis that

$$H_0\colon\ \bar{x}_1 - \bar{x}_2 = 0$$

which means there is no difference between the mean number of letters gained between Fovista + anti-VEGF $(\bar{x}_1)$ and anti-VEGF $(\bar{x}_2)$. The test statistic (t-score) for the Student's t-test for the difference between means is

$$t_{score} = \frac{\bar{x}_1 - \bar{x}_2 - 0}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

where s_1 and s_2 are the standard deviations of the means $\bar{x}_1$ (Fovista + anti-VEGF) and $\bar{x}_2$ (anti-VEGF) and n_1 and n_2 are the sample sizes for the Fovista + anti-VEGF and anti-VEGF arms, respectively. The t_{score} is then converted into a probability (i.e., a p-value) by selecting $n_1 + n_2 - 2$ degrees of freedom as the shape parameter followed by numerical integration.

Exhibit 27

Ophthotech Income Statement

in millions of $ except per share values

Income Statement	FY:11	FY:12	FY:13	FY:14E	FY:15E	FY:16E	FY:17E	FY:18E	FY:19E	FY:20E	FY:21E	FY:22E	FY:23E	FY:24E
GAAP - as reported														
Fovista US Revenue							111	729	1,193	1,514	1,642	1,700	1,755	1,806
Fovista EU Revenue (Novartis Royalty)							8.7	55.6	95.9	112.7	115.9	111.3	105.4	98.3
Novartis Milestones				6.6	140.5	10.5	10.5	10.5	10.5	10.5	60.5	60.5	60.5	60.5
Fovista WW Revenue				6.6	140.5	10.5	130.6	795.1	1,299.3	1,637.0	1,818.5	1,871.9	1,921.2	1,965.1
% change y-o-y							*1140.5%*	*509.0%*	*63.4%*	*26.0%*	*11.1%*	*2.9%*	*2.6%*	*2.3%*
Operating expenses:														
Cost of sales							21.2	138.5	226.6	287.6	312.0	323.0	333.5	343.2
Drug COGS							8.9	56.5	89.5	109.8	114.9	114.8	114.1	112.9
							8.0%	*7.8%*	*7.5%*	*7.3%*	*7.0%*	*6.8%*	*6.5%*	*6.3%*
Royalties							12.2	82.0	137.2	177.9	197.0	208.3	219.4	230.3
COGS + Royalties % of revenue	*n.a.*	*n.a.*	*n.a.*	*0.0%*	*0.0%*	*0.0%*	*16.2%*	*17.4%*	*17.4%*	*17.6%*	*17.2%*	*17.3%*	*17.4%*	*17.5%*
Gross Profit	**0.0**	**0.0**	**0.0**	**6.6**	**140.5**	**10.5**	**109.4**	**656.6**	**1,072.6**	**1,349.4**	**1,506.5**	**1,548.9**	**1,587.7**	**1,621.9**
Gross margin	***n.a.***	***n.a.***	***n.a.***	***100.0%***	***100.0%***	***100.0%***	***83.8%***	***82.6%***	***82.6%***	***82.4%***	***82.8%***	***82.7%***	***82.6%***	***82.5%***
Research and development	13.9	6.8	33.2	66.3	86.9	101.8	96.8	94.1	91.7	89.6	87.8	86.3	85.2	84.4
% of revenue	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*74.1%*	*11.8%*	*7.1%*	*5.5%*	*4.8%*	*4.6%*	*4.4%*	*4.3%*
General and administrative	5.7	6.9	14.2	24.4	25.6	51.9	90.7	113.3	115.9	118.7	121.7	124.8	128.0	131.4
% of revenue	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*n.a.*	*69.5%*	*14.2%*	*8.9%*	*7.3%*	*6.7%*	*6.7%*	*6.7%*	*6.7%*
Others														
% of revenue	*n.a.*	*n.a.*	*n.a.*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Total operating expenses	19.6	13.7	47.4	90.7	112.5	153.7	208.6	345.8	434.2	495.9	521.5	534.1	546.7	558.9
% of revenue	*n.a.*	*n.a.*	*n.a.*	*1377.1%*	*80.0%*	*1459.9%*	*159.8%*	*43.5%*	*33.4%*	*30.3%*	*28.7%*	*28.5%*	*28.5%*	*28.4%*
Operating income/(loss)	**(19.6)**	**(13.7)**	**(47.4)**	**(84.1)**	**28.1**	**(143.1)**	**(99.3)**	**310.7**	**638.4**	**853.5**	**985.0**	**1,014.8**	**1,041.0**	**1,063.0**
Operating margin	***n.a.***	***n.a.***	***n.a.***	***-1277.1%***	***20.0%***	***-1359.9%***	***-76.0%***	***39.1%***	***49.1%***	***52.1%***	***54.2%***	***54.2%***	***54.2%***	***54.1%***
Interest income/(expense)	0.0	(0.5)	(1.5)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gain/(loss) on extinguishment of debt			(1.1)	0.0										
Other income	0.0	0.0	0.0	0.0	0.9	1.2	1.3	0.9	2.5	4.8	7.6	11.0	14.4	17.9
Other gain (loss)	(0.0)	(0.4)	(1.2)	0.0										
Change in fair value related to investor rights liability				0.0										
Net income/(loss) before Taxes	(19.7)	(14.6)	(51.1)	(84.1)	29.0	(141.9)	(97.9)	311.6	640.9	858.2	992.7	1,025.8	1,055.4	1,080.9
Income Tax	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	200.3	300.4	347.4	359.0	369.4	378.3
Effective tax rate (%)	*5.2%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*31.2%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*	*35.0%*
Net income/(loss)	**(18.6)**	**(14.6)**	**(51.1)**	**(84.1)**	**29.0**	**(141.9)**	**(97.9)**	**311.6**	**440.6**	**557.9**	**645.2**	**666.8**	**686.0**	**702.6**
Accretion of preferred stock dividends	(6.8)	(7.1)	(5.9)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income/(loss) to common shareholders	**(25.5)**	**(21.6)**	**(57.0)**	**(84.1)**	**29.0**	**(141.9)**	**(97.9)**	**311.6**	**440.6**	**557.9**	**645.2**	**666.8**	**686.0**	**702.6**
Basic EPS	**($18.27)**	**($14.89)**	**($6.34)**	**($2.60)**	**$0.84**	**($3.96)**	**($2.67)**	**$8.37**	**$11.70**	**$14.65**	**$16.80**	**$17.24**	**$17.66**	**$18.00**
Basic number of shares	1.4	1.5	9.0	32.4	34.4	35.9	36.7	37.2	37.7	38.1	38.4	38.7	38.8	39.0
Diluted number of shares	1.4	1.5	9.0	32.4	35.4	37.1	38.4	39.4	40.5	41.5	42.4	43.2	43.7	44.4

Sources: Oppenheimer Research Estimates, Ophthotech Filings.

Exhibit 28

Ophthotech Balance Sheet

in millions of $ except per share values

Balance Sheet	FY:11	FY:12	FY:13	FY:14E	FY:15E	FY:16E	FY:17E	FY:18E	FY:19E	FY:20E	FY:21E	FY:22E	FY:23E	FY:24E
ASSETS														
Current assets														
Cash and cash equivalents	6.4	4.3	210.6	181.3	239.6	267.7	181.0	499.7	956.2	1,528.9	2,195.8	2,880.9	3,589.2	4,318.2
Prepaid expenses and other current assets	0.1	0.0	6.8	8.0	9.0	12.3	16.7	27.7	34.7	39.7	41.7	42.7	43.7	44.7
Inventory	0.0	0.0	0.0	-	-	-	-	-	-	-	-	-	-	-
Other receivables	1.0			-										
Other Assets		0.3	0.0	196.5	196.5	46.5	46.5	46.5	46.5	46.5	46.5	46.5	46.5	46.5
Security deposits		0.2	0.0	-	-	-	-	-	-	-	-	-	-	-
Total current assets	**7.5**	**4.8**	**217.4**	**385.8**	**445.1**	**326.5**	**244.2**	**573.8**	**1,037.5**	**1,615.1**	**2,284.0**	**2,970.1**	**3,679.4**	**4,409.5**
Property, plant and equipment, net	0.1	0.0	0.0	2.4	4.8	7.8	10.8	13.3	14.8	15.7	16.2	16.3	16.5	16.6
Security deposits (Non-current)	0.2	0.0	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Other long term assets				27.8	27.8	27.8	27.8	27.8	27.8	27.8	27.8	27.8	27.8	27.8
Total assets	**7.7**	**4.9**	**217.7**	**416.2**	**477.9**	**362.3**	**283.0**	**615.2**	**1,080.3**	**1,658.8**	**2,328.2**	**3,014.5**	**3,723.9**	**4,454.1**
LIABILITIES & SHAREHOLDERS' EQUITY														
Accrued clinical drug supplies & trial costs	1.5	1.0	2.5	3.0	3.5	4.1	3.9	3.8	3.7	3.6	3.5	3.5	3.4	3.4
Accounts payable and accrued expenses	1.6	1.4	3.8	4.2	4.7	6.5	8.8	14.5	18.2	20.8	21.9	22.4	23.0	23.5
Accrued bonuses				0.0										
Loans payable, current portion	0.0	0.0	0.0											
Notes payable		11.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Warrant liability	0.2	1.0	0.0	0.0										
Deferred Revenue (Novartis)				173.7	163.1	152.6	142.1	131.6	121.0	110.5	100.0	89.5	78.9	68.4
Deferred Rent	0.0			0.0										
Total current liabilities	**3.3**	**14.4**	**6.3**	**180.8**	**171.3**	**163.1**	**154.7**	**149.8**	**142.9**	**134.9**	**125.4**	**115.3**	**105.3**	**95.3**
Loans payable, less current portion	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Royalty purchase liability		0.0	41.7	83.3	83.3	83.3	83.3	83.3	83.3	83.3	83.3	83.3	83.3	83.3
Total liabilities	**3.3**	**14.4**	**48.0**	**264.2**	**254.7**	**246.5**	**238.1**	**233.2**	**226.3**	**218.3**	**208.7**	**198.7**	**188.6**	**178.6**
Preferred stock														
Series A	65.3	69.5	0.0	0.0										
Series A-1	8.0	8.5	0.0	0.0										
Series B	33.1	35.5	0.0	0.0										
Series B-1	0.5	0.6	0.0	0.0										
Series C			0.0	0.0										
Stockholders' equity (deficit)														
Junior Series A Convertible Preferred Stock	3.0	3.0	0.0	0.0										
Common stock	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Additional paid-in capital		0.0	352.7	410.9	441.2	462.5	475.0	484.4	498.3	507.6	519.9	526.2	533.8	543.2
Accumulated surplus/(deficit)	(105.5)	(126.5)	(183.1)	(259.0)	(218.0)	(346.7)	(430.1)	(102.5)	355.7	932.9	1,599.4	2,289.6	3,001.4	3,732.3
Accumulated other comprehensive income				0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total stockholders' equity/(deficit)	**(102.5)**	**(123.5)**	**169.7**	**152.0**	**223.3**	**115.9**	**44.9**	**382.0**	**854.1**	**1,440.6**	**2,119.4**	**2,815.8**	**3,535.2**	**4,275.5**
Total liabilities & Shareholders equity	**7.7**	**4.9**	**217.7**	**416.2**	**477.9**	**362.3**	**283.0**	**615.2**	**1,080.3**	**1,658.8**	**2,328.2**	**3,014.5**	**3,723.9**	**4,454.1**

Sources: Oppenheimer Research Estimates, Ophthotech Filings.

Exhibit 29

Ophthotech Cash Flow Statement

in millions of US$ except per share values

Cash Flow Statement	FY:11	FY:12	FY:13	FY:14E	FY:15E	FY:16E	FY:17E	FY:18E	FY:19E	FY:20E	FY:21E	FY:22E	FY:23E	FY:24E
Operating cash flows														
Net loss	(18.6)	(14.6)	(51.1)	(84.1)	29.0	(141.9)	(97.9)	311.6	440.6	557.9	645.2	666.8	686.0	702.6
Adjustments														
Depreciation	0.0	0.0	0.0	0.5	1.1	1.9	2.8	3.9	5.0	5.6	6.1	6.4	6.5	6.6
Amortization of debt issuance costs		0.0	0.1	0.0										
Accretion of debt discount		0.1	0.1	0.0										
Non-cash change in fair value of warranty liability	0.0	0.4	1.2	0.0										
Non-cash chg in fair value of investor rights liability				0.0										
Loss on extinguishment of debt			1.1	0.0										
Share-based compensation	0.2	0.6	2.9	10.9	12.0	13.2	14.5	16.0	17.6	19.3	21.3	23.4	25.7	28.3
Pref stk issued for acquired tech & licenses	0.5			0.0										
Accrued int. expense converted to pref stk				0.0										
Changes in operating assets & liabilities														
Prepaid expense and other current assets	0.1	0.0	(6.8)	(1.2)	(1.0)	(3.3)	(4.4)	(11.0)	(7.1)	(4.9)	(2.0)	(1.0)	(1.0)	(1.0)
Other receivables	(0.7)	1.0		0.0										
Inventory	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Security deposits			(0.1)	0.0										
Accrued clinical drug supplies and trial costs	(0.8)	(0.5)	1.5	0.5	0.5	0.6	(0.2)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.0)	(0.0)
Accounts payable and accrued expenses	0.2	(0.2)	2.4	0.4	0.5	1.7	2.3	5.8	3.7	2.6	1.1	0.5	0.5	0.5
Accrued bonuses				0.0										
Deferred revenue				173.7	(10.5)	(10.5)	(10.5)	(10.5)	(10.5)	(10.5)	(10.5)	(10.5)	(10.5)	(10.5)
Deferred rent	(0.0)	(0.0)	0.0	0.0										
Net cash provided by (used in) operating activities	**(19.1)**	**(13.1)**	**(48.8)**	**100.7**	**31.5**	**(138.4)**	**(93.4)**	**315.7**	**449.2**	**569.8**	**661.0**	**685.5**	**707.3**	**726.4**
Investing cash flows														
Purchase of marketable securities				(224.2)										
Maturities of marketable securities	3.4			0.0		150.0								
Purchase of property, equipment	(0.0)		(0.0)	(2.8)	(3.5)	(4.8)	(5.8)	(6.5)	(6.5)	(6.5)	(6.5)	(6.6)	(6.6)	(6.7)
Net cash provided by (used in) investing activities	**3.4**	**0.0**	**(0.0)**	**(227.1)**	**(3.5)**	**145.2**	**(5.8)**	**(6.5)**	**(6.5)**	**(6.5)**	**(6.5)**	**(6.6)**	**(6.6)**	**(6.7)**
Financing cash flows														
Payment of debt issuance costs		(0.4)	(0.0)	0.0										
Proceeds from issuance of common stk	0.0	0.0	0.1	0.0	30.3	21.3	12.5	9.5	13.8	9.3	12.3	6.2	7.6	9.4
Proceeds from initial public offerings, net	0.0	0.0	175.6	0.0										
Proceeds from follow-on public offering, net			0.0	55.4										
(Repayments on) proceeds from notes payables		11.4	(11.9)	0.0										
Repayment of loan payable	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance of preferred stk	15.0		49.7	0.0										
Proceeds from royalty purchase agreement			41.7	41.7										
Net cash provided by (used in) financing activities	**15.0**	**11.0**	**255.1**	**97.1**	**30.3**	**21.3**	**12.5**	**9.5**	**13.8**	**9.3**	**12.3**	**6.2**	**7.6**	**9.4**
Net change in cash & cash equivalents	**(0.7)**	**(2.1)**	**206.3**	**(29.3)**	**58.3**	**28.2**	**(86.8)**	**318.7**	**456.6**	**572.7**	**666.8**	**685.1**	**708.3**	**729.1**
Net cash & cash equivalents - opening balance	7.1	6.4	4.3	210.6	181.3	239.6	267.7	181.0	499.7	956.2	1,528.9	2,195.8	2,880.9	3,589.2
Net cash & cash equivalents - ending balance	6.4	4.3	210.6	181.3	239.6	267.7	181.0	499.7	956.2	1,528.9	2,195.8	2,880.9	3,589.2	4,318.2

Sources: Oppenheimer Research Estimates, Ophthotech Filings.

Stock prices of other companies mentioned in this report (as of 7/3/2014):

Acucela[8] (4589-JP, ¥923, Not Covered)
Advanced Cell Technology (ACTC-OTC, $0.08, Not Covered)
Alexion (ALXN-NASDAQ, $164.21, Outperform)
Alimera (ALIM-NASDAQ, $6.09, Not Covered)
Allergan (AGN-NYSE, $169.13, Not Covered)
Bayer[8] (BAYN.DE-XETRA, €105.10, Not Covered)
GSK (GSK-NYSE, $54.52, Not Covered)
Johnson and Johnson (JNJ-NYSE, $105.42, Not Covered)
Lpath (LPTN-NASDAQ, $3.97, Not Covered)
MorphoSys[8] (MOR.DE-XETRA, €69.85, Not Covered)
Nektar (NKTR-NASDAQ, $13.25, Not Covered)
Novartis (NVS-NYSE, $91.43, Not Covered)
Ohr (OHRP-NASDAQ, $8.12, Not Covered)
Pfizer (PFE-NYSE, $30.53, Not Covered)
Regeneron (REGN-NASDAQ, $311.16, Perform)
Roche[8] (ROG.VX-VTX, CHF268.00, Not Covered)
Santen[8] (4536-JP, ¥5,820, Not Covered)

[8] As of July 4, 2014.

Investment Thesis
We believe Ophthotech's PDGF inhibitor Fovista being developed for wet AMD has high chances of success in an ongoing Phase 3 program (data 2016), with expected FDA approval to follow in 2017. Our conviction is based on solid proof-of-concept from randomized Phase 2 data that showed clear benefits in combination with an approved VEGF inhibitor (standard of care). Upon its commercialization, we see Fovista eventually capturing ~25%/~10% share of US/EU wAMD patients on VEGF therapy and generating peak US/EU sales of ~$1.75B/$500M. Indications for Fovista beyond wAMD (not modeled) and/or proof-of-concept for Phase 2 asset Zimura (we do not value) could generate additional upside.

Price Target Calculation
We value Ophthotech using a discounted cash flow (DCF) analysis with a WACC of 12.5% and a 0% terminal growth rate post-2030, yielding a $95 price target (terminal value of $405M). Our valuation framework utilizes a 12.5% discount rate for pre-commercial stage companies that have achieved clear Phase 2 proof-of-concept.

Key Risks to Price Target
1) Universal failure across all Phase 3 trials or a range of split outcomes (see discussion above pp. 12-13) could jeopardize FDA and/or EMA approval, and/or require additional clinical work that delays cash flows and/or creates an unexpected financing gap. **2)** Although members of management have experience with launching back-of-the eye ophthalmic products (CEO David Guyer was CEO of EyeTech, which developed and launched Macugen), Ophthotech as an independent corporation has yet to establish a commercial infrastructure, distribution capabilities, or market any drug. **3)** Data only in 2016 could mean the stock retains a large discount to our estimated intrinsic valuation, creating risks around opportunity cost. **4)** Share gains among anti-VEGF treated patients could be weaker than projected if cost over Lucentis and Eylea and Avastin and the requirement for a second intravitreal injection emerge as greater headwinds than we currently believe. **5)** More rapid development and approval of competitive PDGF inhibitors, including products possibly co-formulated with existing anti-VEGF agents, could pressure Fovista share. **6)** Regulators could require additional non-clinical trials or require changes to the Phase 3 clinical program for Fovista (endpoints, enrollment criteria, selection of anti-VEGF drugs) that could delay progress of the Phase 3 program relative to the 2016 timeframe for top-line data, magnifying the opportunity cost.

Important Disclosures and Certifications

Analyst Certification - The author certifies that this research report accurately states his/her personal views about the subject securities, which are reflected in the ratings as well as in the substance of this report. The author certifies that no part of his/her compensation was, is, or will be directly or indirectly related to the specific recommendations or views contained in this research report.

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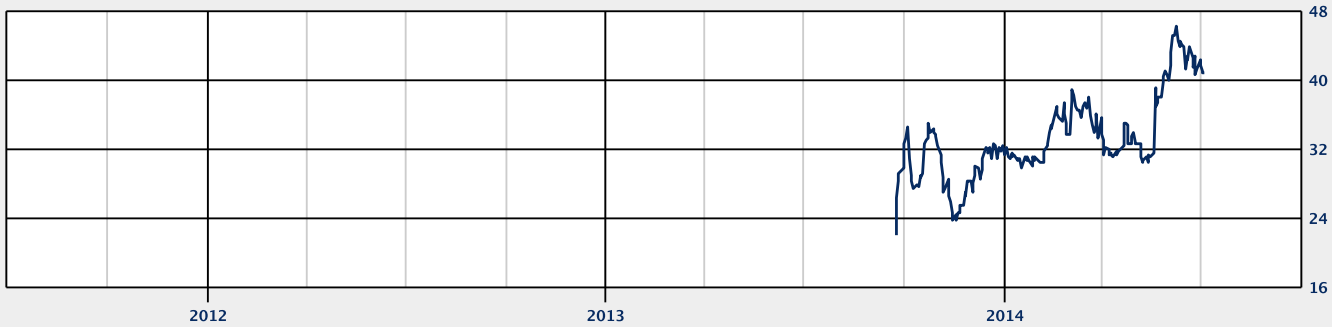
Stock Prices as of July 7, 2014
Alexion Pharmaceuticals (ALXN - NASDAQ, $164.21, OUTPERFORM)
Regeneron Pharmaceuticals (REGN - NASDAQ, $311.16, PERFORM)

Rating and Price Target History for: Ophthotech Corporation (OPHT) as of 07-04-2014



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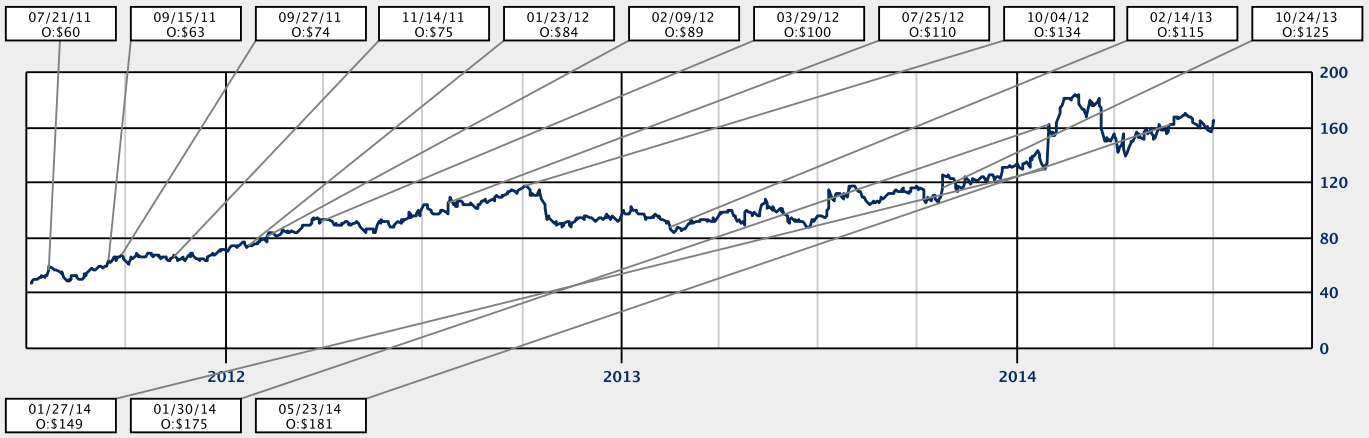
Rating and Price Target History for: Alexion Pharmaceuticals (ALXN) as of 07-04-2014



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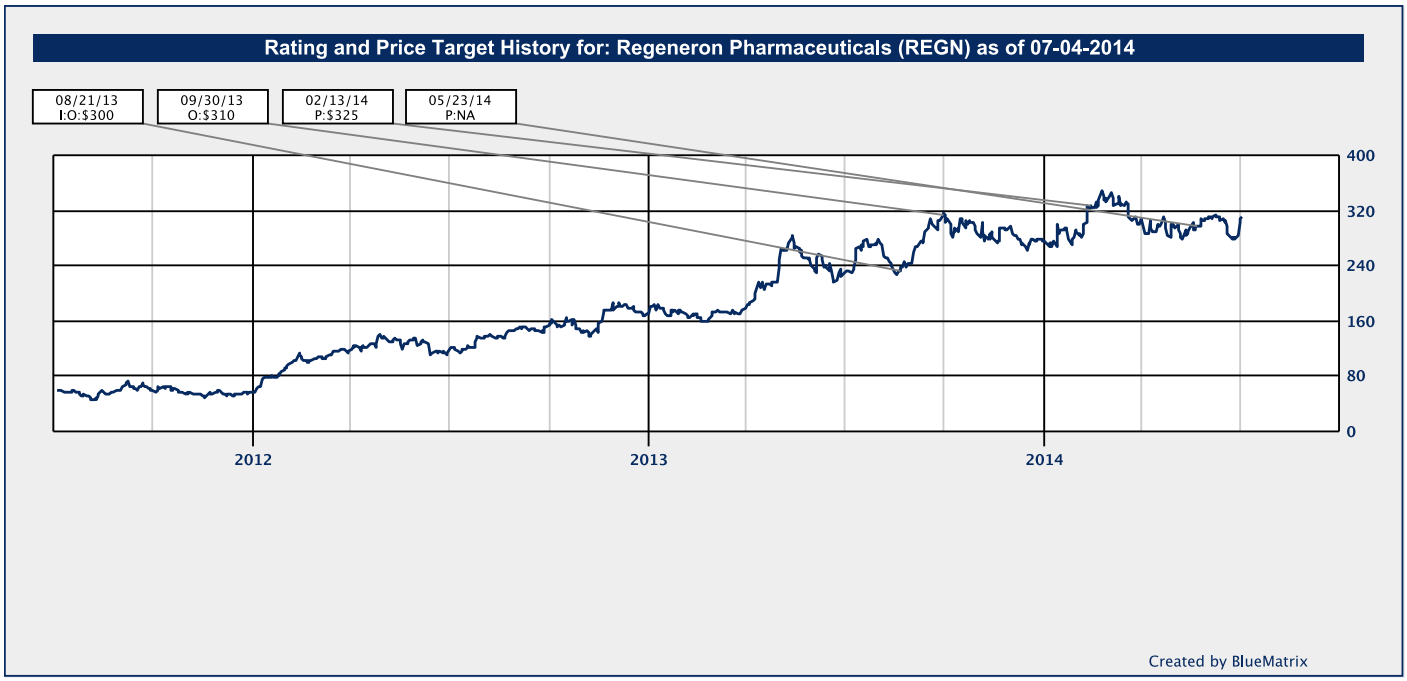

All price targets displayed in the chart above are for a 12- to- 18-month period. Prior to March 30, 2004, Oppenheimer & Co. Inc. used 6-, 12-, 12- to 18-, and 12- to 24-month price targets and ranges. For more information about target price histories, please write to Oppenheimer & Co. Inc., 85 Broad Street, New York, NY 10004, Attention: Equity Research Department, Business Manager.

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Distribution of Ratings/IB Services Firmwide

			IB Serv/Past 12 Mos.	
Rating	Count	Percent	Count	Percent
OUTPERFORM [O]	310	51.75	147	47.42
PERFORM [P]	281	46.91	98	34.88
UNDERPERFORM [U]	8	1.34	2	25.00

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