Initiation
Overweight

OPHT, OPHT US
Price: $29.25

Price Target: $40.00

Ophthotech

Visualizing a Path to Value Creation; Initiating at Overweight

We are initiating coverage of Ophthotech Corp. (OPHT) with an Overweight rating and a Dec 2014 price target of $40. Ophthotech is an ophthalmology-focused biotech with a first-in-class, anti-PDGF aptamer, Fovista, currently in several phase 3 trials for the treatment of wet age-related macular degeneration (wet AMD). We view the large phase 2b dataset of Fovista in combination with Lucentis as significantly de-risking and very predictive of phase 3 success. As such, we expect positive outcomes from the pivotal studies and forecast meaningful adoption of Fovista (~30% market share), which implies a WW market opportunity of almost $2B. Although OPHT shares have fewer near-term catalysts (data expected mid-2016), we still expect the stock to react favorably to phase 3 progress and new clinical studies of Fovista in other indications.

- **Phase 2b Fovista study significantly de-risks the phase 3 program.** In contrast to many early-stage biotechs completing an IPO recently, Ophthotech has a robust phase 2 database with a clinically meaningful result in a trial of almost 450 wet AMD patients. The design of this phase 2b was largely replicated in two ongoing phase 3 trials, which we view as significantly de-risked. Timeline-wise, top-line read-outs from the phase 3 are expected in mid-2016, with FDA approval in 2H17.

- **Combination anti-VEGF/anti-PDGF therapy has the potential to reset efficacy expectations in wet AMD.** In our view, results from the Fovista phase 1 and 2b studies provided support for the view that dual PDGF/VEGF inhibition leads to synergistic clinical effects on both functional (i.e., visual acuity) and physical (i.e., regression in neovascular lesions) endpoints. As such, we expect Fovista to garner broad use in wet AMD given its differentiated activity and improved efficacy beyond the current anti-VEGF paradigm. Indeed, Fovista has the potential to also extend treatment intervals in patients requiring monthly anti-VEGF therapy.

- **Competing anti-PDGF agents are meaningfully behind Fovista, but could provide headline risk.** Ophthotech has a two- to three-year head start, in our view, over other anti-PDGF agents, with nearly all still pre-clinical. That said, as these agents advance, news of their progress could provide headline risk to OPHT shares.

- **Overweight rated; $40 Dec 2014 price target.** On an SOTP basis, we value OPHT at $40/sh, comprising US sales of Fovista at $21/sh, OUS royalties of Fovista at $14/sh, and net cash of $5/sh. Ophthotech's other asset, ARC1905, an early-stage C5 complement inhibitor, should be viewed as source of upside to our models.

Biotechnology

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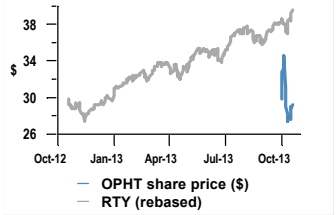
Price Performance



	YTD	1m	3m	12m
Abs	-1.5%	-1.5%	-1.5%	-1.5%
Rel	-29.1%	-5.0%	-7.6%	-34.7%

Ophthotech Corp. (OPHT;OPHT US)

FYE Dec	2012A	2013E	2014E	2015E
EPS ($)				
Q1 (Mar)	-	(1.05)A	(0.49)	-
Q2 (Jun)	-	(1.05)A	(0.51)	-
Q3 (Sep)	-	(1.84)	(0.53)	-
Q4 (Dec)	-	(0.45)	(0.54)	-
FY	(2.52)	(3.48)	(2.07)	(2.26)

Source: Company data, Bloomberg, J.P. Morgan estimates.

Company Data	
Price ($)	29.25
Date Of Price	18 Oct 13
52-week Range ($)	36.00-23.00
Market Cap ($ mn)	906.75
Fiscal Year End	Dec
Shares O/S (mn)	31
Price Target ($)	40.00
Price Target End Date	31-Dec-14

See page 29 for analyst certification and important disclosures.

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J.P.Morgan

Investment Thesis

Ophthotech Corp (OPHT)

Overweight

All eyes on Fovista: first-in-class anti-PDGF represents $2B opportunity

Ophthotech is a biopharmaceutical company focused on the development and commercialization of new therapies for wet AMD. Its lead asset is Fovista, a novel, first-in-class aptamer, agonist with high specificity and affinity against PDGF, a key mediator in the proliferation and survival of abnormal neovascularization – a hallmark of wet AMD. Ophthotech recently initiated a pair of phase 3 trials evaluating Fovista in combination with Lucentis vs. Lucentis in patients with naive AMD, and is set to initiate a third pivotal study in combination with investigator's choice of Eylea or Avastin. Based on the efficacy data from the phase 2b, the combination of an anti-PDGF and anti-VEGF offers potentially best-in-class efficacy with meaningful improvements against the traditional regulatory endpoints of visual acuity, as well as an underappreciated endpoint, regression of neovascularization lesions, against which traditional therapy had minimal effect. Should the phase 3 study successfully replicate the earlier-stage results, we expect Fovista to transform the treatment paradigm for wet AMD and Ophthotech into commercial-stage ophthalmology focused company with a multi-billion dollar franchise.

Phase 2b results significantly de-risk phase 3 outcome, in our view

We believe the phase 3 results have been significantly de-risked based on (1) the statistically significant and clinically meaningful phase 2b results, (2) the fact that the phase 2b study was robust, enrolling more than 440 patients, randomized 2:1 to drug vs. placebo, and (3) the company's aim to replicate the design of the phase 2b in the pivotal studies. As such, in this context, we view our 75% probability of success for the phase 3 study as appropriate.

Forecast meaningful adoption of Fovista, despite complex commercial dynamics

Though the clinical data generated to date have evaluated Fovista in naïve wet AMD patients, we expect the drug will find use in both new starts and, based on our research, as an add-on therapy to patients requiring monthly anti-VEGF injections. Though open-ended questions remain surrounding the treatment interval, duration, willingness of payors to foot the increased cost, and the impact of the anti-VEGF selection, our research indicates positive phase 3 data will ensure the drug finds use in the aforementioned patient segments.

Competing anti-PDGFs lag behind Fovista, but could provide headline risk

While other companies are pursuing anti-PDGF therapies, Ophthotech has a two- to three-year head start, in our view. That said, as these competitors advance their products into the clinic, news of their advancements could provide headline risk to OPHT shares.

Valuation: Overweight rating and $40 December 2014 PT

Our YE'14 price target is based on our SOTP analysis, comprising the contribution from US sales of Fovista ($21/sh), OUS sales ($14/sh) and net cash ($5/sh). That said, we have used a number of conservative assumptions (share, treatment interval, price etc.), which we believe more than account for a lack of catalysts over the nearto midterm. Also, we exclude ARC1905 (C5 complement inhibitor), as well as any

adoption of Fovista outside of wet AMD from our models; any value derived from these sources should be viewed as upside to our estimates.

Risks to Rating and Price Target

Commercial risk

There is no guarantee that the phase 3 results, even if they hit the primary endpoint of the studies, will be viewed as clinically meaningful by clinicians and other stakeholders. Though we believe the phase 3 data will be supportive of approval and position the combination as the new gold standard, commercial adoption might still be impeded by the cost of the combination (i.e., Fovista plus Lucentis or Eylea), the dosing frequency in the phase 3 studies, and/or the underlying dynamics of the anti-VEGF market. Indeed, the question of how Fovista will be incorporated into the treatment paradigm for wet AMD remains the primary risk to our investment thesis.

Clinical risk

Clinical trials can be difficult to predict. Though we are encouraged by the positive and robust data set from the Fovista phase 2b study in wet AMD, these results need to be confirmed in the pivotal phase 3 studies. There is no guarantee that the Fovista phase 3 program will be successful and/or replicate the outcome of the phase 2b studies. Additionally, Ophthotech's pipeline beyond Fovista is relatively early in clinical development.

Regulatory risk

Ophthotech has indicated that it intends to file an NDA for Fovista based on the outcome of the phase 3 results, which are expected to read out in mid-2016. Though we anticipate successful phase 3 results would be adequate for regulatory agencies in the US and Europe, there is no guarantee that the current development plan will be sufficient for regulators, and that additional studies or analyses will not be required, potentially delaying approval.

Financial risk

With the completion of the IPO, Ophthotech has approximately $230M in cash and short-term investments. In addition, Ophthotech has the option of drawing down the additional two individual tranches of $41.6M related to its royalty sale agreement with Novo A/S. Though these resources should be adequate for the company to complete its phase 3 studies, the company will likely need to revisit the capital markets again at some point in the future. Future financings will dilute existing shareholders, which could negatively impact share price.

Intellectual property risk

Ophthotech holds a composition of matter patent on Fovista that does not expire until 2017. Should Fovista be approved, we expect the company to pursue a Hatch-Waxman extension, potentially delaying expiry of the relevant patent until 2022. Additionally, the company has use patents covering Fovista plus Lucentis or Avastin until 2024. Though we expect manufacturing and the proprietary nature of the Fovista PEG moiety provided by Nektar to provide meaningful hurdles to a generic entrant, there is no guarantee the company will be successful and may face a generic

entrant as early as 2017 in the US. Such a development would negatively affect the value of Fovista and OPHT shares.

Company Description

Ophthotech Corporation is a biopharmaceutical company specializing in the development of novel therapeutics to treat diseases of the eye. Fovista, the company's lead asset, is a novel anti-PDGF pegylated aptamer being developed for use in combination with anti-VEGF agents for the treatment of wet age-related macular degeneration (wet AMD). Ophthotech successfully completed a phase 2b study in which Fovista plus Lucentis demonstrated superior efficacy, as measured by mean change in visual acuity from baseline at 24 weeks, versus Lucentis alone. Ophthotech recently initiated the first of three phase 3 studies designed to support an NDA. Top-line data on the primary endpoint (mean change in visual acuity from baseline at 52 weeks) from these trials are expected in mid-2016. Ophthotech has also identified a number of smaller trials in high unmet needs (e.g., anti-VEGF resistant AMD, von Hippel-Lindau) in which the company may evaluate use of Fovista in phase 2 studies beginning in 2014. These studies, which have yet to be finalized, would be expected to read out in 2015. Beyond Fovista, Ophthotech also has ARC1905, a pegylated aptamer targeting the C5 component of the complement cascade, in phase 1/2 studies for wet AMD.

Overview

Background

New York-based Ophthotech was founded in 2007 by Dr. David Guyer and Dr.Samir Patel, former executives at Eyetech who were responsible for the development of Macugen, an anti-VEGF aptamer and the first approved targeted therapy for wet AMD. Drs. Guyer and Patel were also responsible for the sale of Eyetech to OSI Pharmaceuticals (now Astellas; covered by JPM analyst Masayuki Onozuka) for $935M (75/25 cash and stock) in 2005. Shortly thereafter, OSI reprioritized its efforts, narrowed its focus to oncology, and pursued divestment of its assets in ophthalmology, including a pre-clinical anti-PDGF aptamer, then known as E10030 (now Fovista), which it had acquired as part of the Eyetech acquisition.

In conjunction with its founding, Ophthotech raised $36M from three venture capital firms and in-licensed two aptamer based products: Fovista from OSI and a C5 complement inhibitor, ARC1905, from Archemix.

Since that time, Ophthotech has identified Fovista as the lead asset, completing a phase 1 and 2b study with the drug in wet AMD. In 3Q13, Ophthotech initiated a pair of pivotal phase 3 studies with the drug in combination with Lucentis. These trials aim to replicate the results of a phase 2b study and are expected to support approval. An additional study evaluating Fovista in combination with Eylea/Avastin in wet AMD is set to begin by YE13/1Q14. A phase 2 study of ARC1905 is also planned to initiate in wet AMD in 2014.

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Pipeline, Catalysts and Milestones

The Ophthotech portfolio is primarily focused on the clinical development of Fovista. In addition to Fovista, Ophthotech also holds the rights to ARC1905, an aptamer directed against the C5 complement protein for the treatment of wet AMD. The pipeline is detailed in Table 1.

Table 1: Ophthotech Pipeline

Product	Indication	PC	Ph 1	Ph 2	Ph 3	Marketed
Fovista	Wet AMD (combo w/ Lucentis)					
Fovista	Wet AMD (combo w/ Eylea / Avastin)					
ARC1905	Wet AMD					

Source: Company reports.

Ophthotech has minimal key catalysts over the next 18 months as the company focuses on the execution of its phase 3 trials for Fovista. The company intends to initiate a third phase 3 study of Fovista in YE13/1Q14, while additional studies that may broaden the drug's potential label (e.g., wet AMD patients no longer responsive to anti-VEGF therapy, retinal manifestations of von Hippel-Lindau disease, etc.) are expected to be disclosed in 2014. Upcoming catalysts and milestones for the company are reviewed below in Table 2.

Table 2: Upcoming Catalysts for Ophthotech

Timing	Drug	Event	Significance
Nov 16-19	-	American Academy of Ophthalmology (New Orleans)	Medium
YE13/1Q14	Fovista	Initiate combination study in wet AMD with Eylea / Avastin	Medium
4Q13/1H14	-	Regeneron launches phase 1 study with anti-PDGF mAb	High
2014	ARC1905	Initiate phase 2 study in wet AMD	Low
2014	Fovista	Initiate study in setting other than naïve wet AMD	Medium
1H15	Fovista	Complete enrollment of phase 3 trials	High
2015	ARC1905	Read out of phase 2 study in wet AMD	Medium
Mid-2016	Fovista	Read-out of pivotal combination studies in wet AMD	High
2H16	Fovista	Submit NDA for wet AMD	High

Source: Company reports.

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Fovista (E10030) for Wet AMD

Summary

Ophthotech's lead asset, Fovista, is a pegylated aptamer and a highly specific agonist against platelet-derived growth factor (PDGF), a key mediator of angiogenesis. The drug acts by binding to PDGF, preventing interaction with the PDGF-receptor, and eventual death of pericytes. Fovista is being developed for the treatment of wet AMD in combination with existing anti-VEGF therapies. In a phase 1 and phase 2b study, the combination of Fovista and Lucentis achieved clinically significant gains in visual acuity versus Lucentis monotherapy alone. Additionally, the combination also achieved dramatic regressions in neovascular lesions. Based on these results, Ophthotech has launched a comprehensive phase 3 program comprised of two phase 3 trials evaluating the combination of Fovista and Lucentis vs. Lucentis monotherapy, and a third trial comparing the combination of Fovista plus the choice of Eylea/Avastin vs. Eylea/Avastin alone.

We view the phase 2b results (improvement in visual acuity and reductions in CNV) as compelling given the robustness of the study design (i.e., number of patients, Lucentis comparator). Given this, we believe the phase 3 pivotal trials have been significantly de-risked and expect the drug to be approved and integrated into the wet AMD treatment paradigm, driving meaningful adoption (~30% market share). Top-line read-out of the phase 3 pivotal studies is expected in mid-2016, followed by an NDA submission before YE16. We model a formal US launch by YE17 and forecast worldwide sales at peak of ~$1.7B.

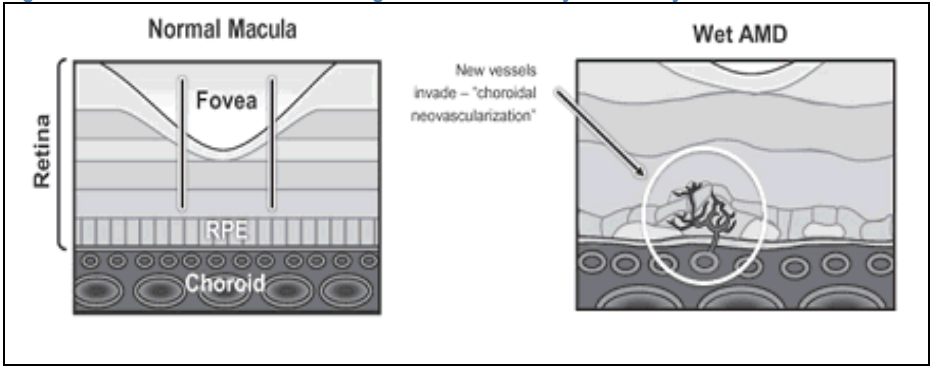
Primer on AMD Biology

Age-related macular degeneration (AMD) is a disorder of the posterior segment of the eye and is characterized by progression from asymptomatic accumulation of extracellular aggregates (called drusen) leading to visual impairment and, potentially, blindness. Indeed, AMD is the leading cause of blindness in the US and most Western nations. The disease manifests in two distinct forms, wet or dry AMD, distinguished by the presence or absence of neovascularization.

In the case of wet AMD, the disease is defined by the presence of abnormal angiogenesis (i.e., blood vessel growth), clinically referred to as choroidal neovascularization (CNV). Abnormal vessels sprout from the choriocapillaris (the vascular layer of the eye) under the retinal pigment epithelium (RPE). CNV results in vision loss as new vessels commonly leak serous fluid, protein and blood, which over time leads to scarring of the retina (see Figure 1).

This proliferation and invasion of abnormal blood vessels in wet AMD represents a complex process orchestrated by a diverse set of signaling pathways, growth factors, cytokines, and associated receptors. Two leading mediators of the cascade of events are (1) vascular endothelial growth factor (VEGF) and (2) platelet-derived growth factor (PDGF). The relationship between VEGF, PDGF, and the structural biology of blood vessels is critical to understanding the current approach to treating AMD, as well as the scientific rationale behind Ophthotech's approach with Fovista.

Figure 1: Cross-Section of Posterior Segment in a Normal Eye and an Eye with Wet AMD



Source: Ophthotech S-1 filing

New blood vessels comprise two distinct cell types: endothelial cells and perivascular cells (or pericytes). Endothelial cells form the inner lining of the vessel wall, release PDGF, and express VEGF receptors (VEGFR), which bind VEGF-promoting cell survival and proliferation. In contrast, perivascular cells line the outside of blood vessel providing structure and vascular stability.[1,2]

In wet AMD, activated endothelial cells form angiogenic sprouts from existing vessels in the direction of VEGF concentration gradients. These vessels are initially unstable and leaky.[3] To facilitate their maturation, endothelial cells secrete PDGF in order to promote migration of pericytes, which express receptors specific for PDGF (PDGFR). As such, it has been demonstrated that pericytes and endothelial cells engage in a paracrine mode of action during angiogenesis.[2,4]

Anti-VEGF therapy has proven the most tractable approach to date for treatment of wet AMD. Lucentis, Avastin and Eylea all bind to the VEGF-a, blocking the interaction with cell surface receptor, inhibiting endothelial cell proliferation, survival and vascular permeability. The clinical development of Fovista has been based on the view that by stripping blood vessels of pericytes, endothelial cells will be left "unprotected," that the paracrine loop of interaction will be disrupted, and that blood vessels will be left more vulnerable to the effects of anti-VEGF drugs. In preclinical models, administration of the synergistic effects of dual anti-PDGF/anti-VEGF therapy includes stripping of pericytes in abnormally proliferating blood vessels.[5]

Current Therapeutic Paradigm in Wet AMD

As noted above, the current standard of care in wet AMD focuses on the administration of anti-VEGF agents via regular intravitreal injections into the retina. Currently there are three approved anti-VEGF agents: Pfizer's Macugen, Roche/Genentech's Lucentis, and Regeneron's Eylea. However, Roche/Genentech's Avastin is used on an off-label basis and still commands a majority share in the US,

[1] Allt G, Lawrenson JG Cells Tissues Organs 2001; 169:1–11
[2] Hellstrom M J Cell Biol 2001; 153:543–553
[3] Benjamin LE Development 2008; 125:1591–1598
[4] Hellstrom M Development 1999;126:3047– 3055
[5] Jo N et al. Am J Pathol 2006;168:2036–2053

with Eylea and Lucentis garnering the remaining use (see Table 3).[6] (Note: JPM analysts Chris Schott and Richard Vosser cover Pfizer and Roche, respectively.)

The current treatment paradigm in wet AMD is to initiate treatment with the goal of halting exudation and extending the interval between treatments (i.e., "treat and extend"). After beginning monthly anti-VEGF injections, patients are typically reassessed at the 3-6 month mark, whereby the decision is either made to "extend" the dosing interval, usually to 6-8 weeks, or monthly dosing is continued. For those patients continuing monthly-interval dosing, their progress continues to be monitored. In the cases where patients have inadequate responses with monthly dosing, ophthalmologists will often switch to a different anti-VEGF therapy (e.g., switching from Avastin to Lucentis, Lucentis to Eylea, or Avastin to Eylea).

Table 3: Anti-VEGF Therapies Used for the Treatment of Wet AMD

Treatment	Company	FDA Approval	2012 WW Sales
Eylea	Regeneron (US) / Bayer (ex-US)	Sept 2012	$855M
Lucentis	Roche / Genentech (US) / Novartis (EU)	June 2006	$3,828M
Avastin	Roche / Genentech (US)	Used off-label	-

Source: FDA.gov, Company reports

In terms of choosing an initial anti-VEGF therapy, our research indicates that new patients are typically being initiated on Avastin or Eylea, and to a lesser extent on Lucentis. That said, a meaningful percentage of patients remain on Lucentis, having started therapy prior to the approval of Eylea.

Table 4: Comparison of Visual Acuity Gains in Selected Wet AMD Trials at 1 Year

	VIEW1[7]	VIEW2[7]	MARINA[8]	ANCHOR[9]	CATT[10]
Design	Eylea Q4W v. Eylea Q8W v. Lucentis Q4W	Eylea Q4W v. Eylea Q8W v. Lucentis Q4W	Q4W Lucentis Q4W v. Sham Inj.	Q4W Lucentis Q4W v. sham Inj.	Avastin Q4W v. Lucentis Q4W v. Avastin PRN v. Lucentis PRN
Size (n=)	909	906	716	423	1208
Mean change in VA from baseline (at 52w)	7.6 / 10.9 / 8.1	8.9 / 7.6 / 9.4	11.0 / -8.5	6.3 / -11.9	8.0 / 8.5 / 5.9 / 6.8
Gain in VA (>15 letters) at 52w (% of patients)	31 / 38 / 31	31/ 29 / 34	37 /11	31 / 6	31 / 34 / 28 / 25
Visual acuity maintained (Loss of <15 letters) at 52w (% of patients)	94 / 95 / 94	95 / 95 / 95	98 / 66	91 / 60	94 / 94 / 92 / 95

All data shown for Lucentis is the 0.5mg dose
Source: Company reports.

Despite the availability of three agents, there remain meaningful unmet needs in the treatment of wet AMD. Of note, current therapies have increased the mean visual acuity by ~6-10.6 letters at 6 months (data not shown) with limited additional gains out to 1 year with gains 6.3-11.0 letters (see Table 4). Additionally, ~22-34% of patients at 6 months (data not shown) and ~25-38% at 1 year (see Table 4)

[6] Regeneron 2Q13 earnings call
[7] Heier JS et al., Ophthalmology. 2012 Dec;119(12):2537-48
[8] Rosenfeld PJ et al., N Engl J Med. 2006;355:1419-1431
[9] Brown DM et al., Ophthalmology. 2009 Jan;116(1):57-65
[10] CATT Research Group et al., N Engl J Med. 2011 May 19;364(20):1897-908

experience a significant gain of ≥15 letters. Though the available therapies have significantly reduced the loss of visual acuity at the - year mark, the majority of patients (~60-70%) do not achieve significant vision gains. Further, there remains a significant portion of patients who require monthly injections, creating a high burden on both patients, caregivers and the overall system. Additionally, a segment of patients (~25% by our research) lose vision by the 1-year mark.

Emerging Approaches to Wet AMD

Emerging approaches to wet AMD have generally fallen into one of three categories: (1) anti-VEGF agents attempting to extend the duration interval, (2) novel anti-angiogenic targets, primarily anti-PDGF, or (3) agent taking an orthogonal approach the disease by targeting inflammation, typically at steps in the complement cascade. We detail selected emerging agents in Table 5.

In terms of extending the duration interval, various approaches have been attempted ranging from optimized mAbs (e.g., Eylea) to long-acting implants and gene therapy approaches. Other than Eylea, these approaches have been largely unsuccessful. The most promising of the remaining approach is the DARPin platform from Allergan (covered by JPM analyst Chris Schott). However, based on updates from Allergan earlier this year. it appears that this approach may not offer differentiation from Eylea, and a decision on moving into more advanced phase 2 studies has been delayed. Additional data on the initial phase 2 study will be presented at AAO next month (November 16-19; New Orleans).

Of the emerging anti-PDGF agents in the clinic, we call particular attention to Regeneron's pre-clinical anti-PDGF mab, which is expected to enter the clinic this year and Allergan's dual-targeting anti-PDGF/anti-VEGF DARPin, which is expected to enter the clinic next month. Also, Xcovery Vision has a dual-targeting anti-PDGF/anti-VEGF agent in an ongoing phase 1. Given that it is an oral agent, we remain skeptical of its potential efficacy or potential commercial adoption by ophthalmologists.

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Table 5: Selected Emerging Competition in Wet AMD

NOVEL ANTI-ANGIOGENIC AGENTS				
Drug	**Target**	**Company**	**Status**	**Comments**
Fovista	PDGF	Ophthotech	Phase 3	Phase 3 studies started 3Q13. Data expected mid-2016.
X-82	PDGF/VEGF	Xcovery Vision	Phase 1	Phase 1 ongoing in 20 patients. Expected to read out in 2H14 (oral administration makes us skeptical).
PDGFR mAb	PDGF/VEGF	Regeneron	Pre-Clinical	Will be co-formulated with Eylea. Ph 1 expected to start 4Q13.
DARPin	PDGF/VEGF	Allergan	Pre-Clinical	Expected to enter clinic in 2014 (most promising, but may not be differentiated from Eylea).
NT-506	PDGF	Neurotech	Pre-Clinical	PDGF antagonist leveraging company's encapsulated cell technology implant.
Undisclosed	PDGF	Somalogic	Pre-Clinical	Anti-PDGF SOMAmer.

ANTI-VEGF THERAPIES				
Drug	**Formulation**	**Company**	**Status**	**Comments**
AGN-150998	DARPin	Allergan	Phase 2	▪ Allergan announced on its 1Q13 earnings call that the first portion of the Phase 2 REACH study had been completed and that there was a lack of differentiation to Lucentis. 1-2 year delay in potential approval; phase 3 was previously expected to start by YE13. ▪ Phase 2 REACH results will be presented at AAO in Nov 2013.

Source: Compnany reports, biomedtracker

Clinical Development of Fovista

The clinical development of Fovista has to date been focused solely on the treatment of wet AMD, comprising two completed studies (phase 1 study OPH1000 and phase 2b study OPH1001), two recently initiated pivotal phase 3 studies in combination with Lucentis (OPH1002 and OPH1003), and another soon to be initiated phase 3 study (OPH 1004) in combination with investigator's choice of Eylea or Avastin (see Table 6).

Table 6: Clinical Development Program for Fovista

Trial	Design	Population	Size	Endpoint	Comments
Phase 1 (OPH1000)	Fovista + Lucentis	Naïve wAMD	22	Safety	• 59% of pts achieved ≥15-letter gain in BCVA at week 12 • 86% mean reduction in size of CNV lesion • 91% of pts achieved partial reduction in CNV size • Clean safety profile
Phase 2b (OPH1001)	Fovista + Lucentis vs. Lucentis	Naïve wAMD	449	Mean change in BCVA at week 24	• 62% benefit in mean change in visual acuity from baseline at week 24 • 27% benefit in patients achieving >3-line improvement (36% vs. 29%) • Retrospective analysis highlighted meaningful improvement in regression of CNV size at just 24 weeks
Phase 3 (OPH1002)	Fovista + Lucentis vs. Lucentis	Naïve wAMD	622	Mean change in BCVA at week 24	• Trial initiated August 2013 • Data expected mid-2016
Phase 3 (OPH1003)	Fovista + Lucentis vs. Lucentis	Naïve wAMD	622	Mean change in BCVA at week 24	• Trial initiated August 2013 • Data expected mid-2016
Phase 3 (OPH1004)	Fovista + Eylea/Avastin vs. Eylea/Avastin	Naïve wAMD	622	Mean change in BCVA at week 24	• Trial expected to initiate 4Q13/1Q14

wAMD = wet AMD

Source: Company reports, cliinicaltrials.gov

Outside of the currently disclosed phase 3 studies, Ophthotech has also disclosed that it may plan additional studies in patients with wet AMD who had an inadequate response to existing anti-VEGF therapy, as well as rare-disease populations such as proliferative vitreoretinopathy, and the retinal manifestation of von Hippel-Lindau. We do not expect to hear incremental details on any or all of the above-defined studies until 2014.

Phase 1 results

In 2009, Ophthotech initiated a phase 1, multi-center, open-label, ascending dose, clinical study with Fovista, enrolling 22 patients with treatment naïve wet AMD to one of four doses (0.03, 0.3, 1.5, and 3.0mg doses) of the drug in combination with

Lucentis. Fovista and Lucentis were administered once monthly for 12 weeks. The combination was well tolerated with no dose-limiting toxicities or safety concerns observed.

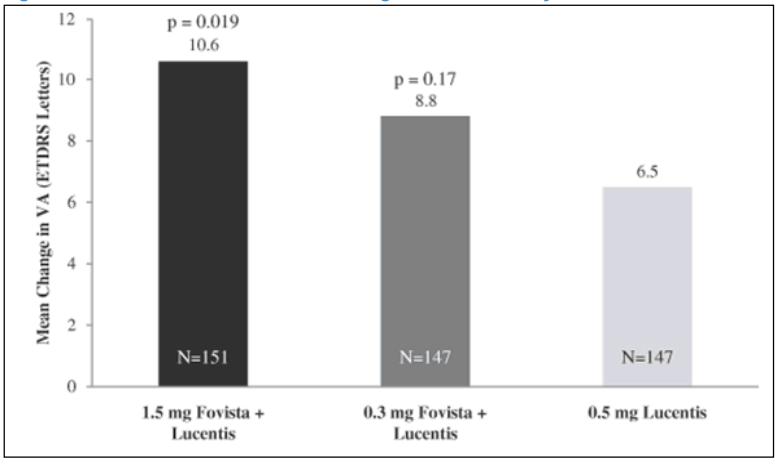
In terms of efficacy, the trial provided the first clinical evidence of synergistic activity between anti-VEGF and anti-PDGF therapy, while also achieving dramatic reductions in the size of choroidal neovascularization (CNV) lesions, clearly differentiating the combination from anti-VEGF monotherapy.[11]

Specifically, the combination led to meaningful improvements in visual acuity (59% of patients achieved a gain of ≥15-letters in best corrected visual acuity at week 12 compared with historical controls of ~33% on anti-VEGF monotherapy). Additionally, the phase 1 also demonstrated robust reductions in CNV lesions with mean reduction of 86% from baseline. Further, no patients receiving combination therapy experienced progression of CNV in the trial.

Phase 2b results

Based on the suggestions of activity in the phase 1 study, Ophthotech initiated a robust phase 2b trial, enrolling 449 patients in randomized, controlled, six-month study evaluating the combination of Fovista (at two doses 0.3mg and 1.5mg) and Lucentis to Lucentis alone in patients with naïve wet AMD. The study met its primary endpoint (mean change in visual acuity from baseline at Week 24) achieving a statistically significant 62% comparative improvement with the combination vs. Lucentis alone (1.5mg combo: 10.6 letters vs. 6.5 with Lucentis alone; the lower dose combination achieved an 8.8 letter gain from baseline, which missed statistical significance vs. placebo).[12] The results are detailed in Figure 2. In interviews with clinicians, one offered, *"The four-letter gain is meaningful and respectable. Lucentis is a very high bar to beat. If you assume all the anti-VEGF are basically the same in terms of efficacy, which most retinal specialist do, this is essentially best in class."*

Figure 2: Phase 2b Results – Mean Change in Visual Acuity from Baseline at 24 Weeks



Source: Ophthotech S-1 filing

In reviewing the results of the phase 2b study, we believe there are a number of key takeaways. First, the combination beat a high bar in Lucentis monotherapy (see

[11] Boyer DS, Invest Ophthalmol Vis Sci Online ARVO abstract 1260
[12] Boyer DS, May 5-9, 2013; Seattle, Washington. Abstract 2175.

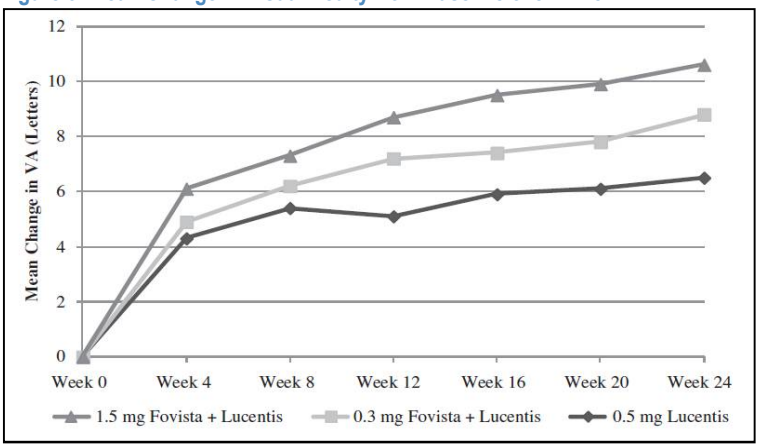
Table 4). Recall, no previous regimen has demonstrated statistically significant superiority to Lucentis monotherapy in terms of visual acuity. Next, the improvements were consistent against key secondary endpoints (e.g., patients achieving >15letter gains) measured at week 24. Two points associated with these data are particularly impressive: (1) Fovista's demonstrated efficacy on secondary endpoints was in line with historical 52-week anti-VEGF monotherapy data (see Table 7), and (2) the Fovista data appears to be improving, rather than plateauing, at 24 weeks (see Figure 3). This is important in that this contrasts nicely with perceptions with anti-VEGF monotherapy, which is commonly viewed to plateau at around 3-6 months. Another clinician offered, *"We usually know what we are going to get by six months with a therapy. Showing improvement, or at least a ramp prior to the six-month mark, gives me hope that patients will continue to improve in a longer study."*

Table 7: Phase 2b Fovista (1.5mg Dose) Data vs. Historical Anti-VEGF Therapy Data

	Phase 2b Fovista Study	Historic Controls for anti-VEGF Therapy
Mean change in VA from baseline (letters)	10.6 at 24 weeks	8-10 at 52 weeks
Gain in VA (>15 letters) at 12 and 24 weeks (% of patients)	32% at 12 weeks 39% at 24 weeks	30-40% at 52 weeks

Source: Company reports and J.P. Morgan analysis

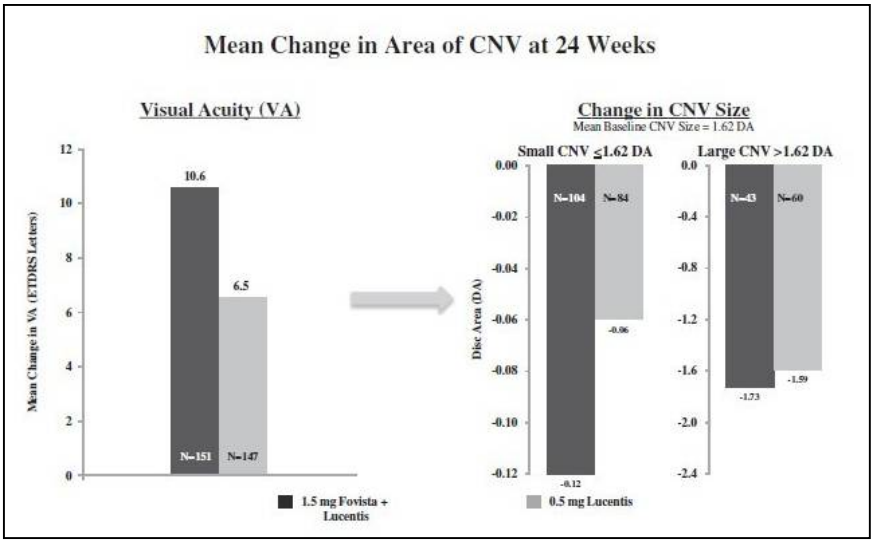
Figure 3: Mean Change in Visual Acuity from Baseline over Time



Source: Company reports.

The combination also demonstrated greater reduction in CNV size than with Lucentis monotherapy alone, based on a retrospective analysis of the data (see Figure 4), when patients were stratified by CNV size at baseline. One interviewee offered on the data, *"Reducing the size of lesions is important even if it hasn't impacted visual acuity by week 24. There is more to vision than just visual acuity, and reducing the size of these lesions is important. It's been underemphasized only because the anti-VEGFs have minimal effects on this aspect."* Another offered, "*This is the one area where anti-VEGF monotherapy would not be competitive.*"

Figure 4: Mean Change in Area of CNV at 24 Weeks



Source: Company reports.

Pivotal phase 3 studies

Based on the phase 2b results, Ophthotech initiated a pair of phase 3 studies, each pursuing a similar design to the phase 2b study. 622 patients will be enrolled into each study, randomized 1:1 to Fovista plus Lucentis or Lucentis alone. Patients will be followed for two years, but the primary endpoint will be mean changes in visual acuity from baseline at 52 weeks. The study will look at a similar set of secondary endpoints to the phase 2b results, including the percent of patients with >15-letter gains and losses, regressions in CNV size, etc. The studies are expected to read out top-line results in mid-2016.

Additionally, the company is also expected to initiate shortly another phase 3 study evaluating Fovista plus investigator's choice of Eylea or Avastin vs. Eylea or Avastin alone. The endpoints and timeline for the studies are similar to the other pivotal studies.

Market Projections for Fovista

Our model for Fovista focuses exclusively on the wet AMD opportunity in combination with anti-VEGF therapy in the US and EU; use in other indications, geographies, or as a monotherapy should be viewed as upside to our estimates. Based on discussions with clinicians and industry contacts, we estimated that ~10% of 2.1 million and 2.6 million cases of advanced AMD in the US and EU, respectively, have wet AMD, and that 40% of patients have bilateral disease, to arrive at an addressable wet AMD eye prevalence of ~300,000 in the US and ~443,000 in the EU.

From this point, we spent considerable time speaking with clinicians and industry contacts on the adoption and prescription dynamics based on the phase 2 study, including (but not limited to) how clinicians will segment their patient population at the time of launch, the impact (if any) of current anti-VEGF therapy on patients switching, and the role of cost in the treatment decision. Clinicians unanimously believed that should the phase 2 results hold up in the phase 3 study and the drug be approved that it will find use at least in a segment of their naïve patients initially. From that point, clinicians stated that their personal experiences with the drug in this setting would be the critical factor in driving use in areas outside the clinical trials, new investigator sponsored trials (ISTs) notwithstanding. The next area of focus for prescribers will be patients who are stable but who are unable to extend beyond a monthly dosing interval. We focused on these two segments for our model. Additional comments on the value proposition by patient segment are summarized in Table 8.

Table 8: Patient Segmentation

Segment	Size of Patient Population in Practice	Value Proposition / Comments
Naïve (started therapy within 12mos)	10-20%	**Combination offers potentially best available therapy to prevent vision loss** Initial patient segment that will be prescribed Fovista Questions remain over duration and ability to extend treatment interval
Stable on Monthly Interval	20-40%	**Potentially may extend treatment interval** No data currently to support view that Fovista will extend treatment interval Expected to be early area of experimentation and ISTs for clinicians
Stable on Extended Interval	40-60%	Less need to shift therapy or willingness to add-cost, unless patient is losing vision
Non-responders to anti-VEGF therapy	1 - 10%	**Interest in exploring use of Fovista either as monotherapy or in combination with anti-VEGF** Limited data thus far to support use in this population Relatively small number of patients; Cycling VEGFs usually generates at least some response Re-sensitization of patients to anti-VEGFs after therapy with Fovista would be huge win

Source: J.P. Morgan analysis

The two patient segments identified above represent, at any one point, in a retinal specialist's practice (based on our interviews) 30-50% of patients. Given the lack of data to address the projected duration of therapy or dosing interval with Fovista, we conservatively forecast a peak market share of ~30% for Fovista/anti-VEGF combination therapy, and assumed a treatment duration of ~12 months, and 6-7 injections per affected eye. We structured our market similar in the EU as well. Further, we made, in our view, conservative assumptions regarding price (US:$1,400 per vial; EU: $1,000) at launch.

Based on these assumption, we forecast a launch in the US in 2H17 leading to $188M in sales in that year, an EU launch in FY18 with sales growing to $534M in 2018, $860M in 2019, $1.2B in 2020, and to $1.7B in 2024 (see Table 9). In 2024, we forecast US sales of $899M (Table 10) and EU sales of $837M (Table 11).

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Table 9: WW Fovista Sales Forecast

WW Summary	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Fovista summary	**188**	**534**	**859**	**1,236**	**1,456**	**1,637**	**1,701**	**1,736**
US	188	425	548	687	784	881	890	899
EU	-	109	311	549	672	756	811	837
Growth Rates	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**
Fovista	na	184%	61%	44%	18%	12%	4%	2%

Source: J.P. Morgan estimates.

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Table 10: AMD US Market Model (2017- 24E)

Wet AMD US Market Model	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Diagnosed Prevalence of Adv. AMD, US (000s)	2,273	2,295	2,319	2,346	2,371	2,397	2,422	2,447
% pts wet AMD	10%	10%	10%	10%	10%	10%	10%	10%
% with bilateral disease	40%	40%	40%	40%	40%	40%	40%	40%
Addr. Pop - Eyes with wAMD (000s)	318	321	325	328	332	336	339	343
Treatment Paradigm Structure								
% Treated with anti-VEGF monotherapy	90%	82%	77%	73%	69%	66%	66%	66%
% Treated with combo (anti-VEGF + anti-PDGF)	7%	14%	18%	23%	27%	30%	30%	30%
% Treated with anti-PDGF monotherapy	0%	0%	0%	0%	0%	0%	0%	0%
% Treated	97%	96%	95%	96%	96%	96%	96%	96%
% Treated with anti-PDGF	7%	14%	18%	23%	27%	30%	30%	30%
VEGF Market Share	96.5%	95.5%	95.0%	96.0%	96.0%	96.0%	96.0%	96.0%
Avastin	40%	40%	40%	40%	40%	40%	40%	40%
Lucentis	23%	23%	22%	22%	21%	21%	20%	20%
Eylea	37%	38%	38%	38%	39%	39%	40%	40%
Patients on Therapy								
Total treated patients (000s)	**307**	**307**	**308**	**315**	**319**	**322**	**326**	**329**
Fovista (000s)	21	43	58	76	90	101	102	103
VEGF Treated (000s)	307	307	308	315	319	322	326	329
Avastin	123	123	123	126	127	129	130	132
Lucentis	71	69	68	68	68	67	66	66
Eylea	114	115	117	121	124	126	129	132
Pricing Analysis (USD)								
Avastin, per vial	$ 59	$ 59	$ 59	$ 59	$ 59	$ 59	$ 59	$ 59
Price increases	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Mean Number of injections/year	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5
Lucentis, per vial	$ 1,950	$ 1,950	$ 1,950	$ 1,950	$ 1,950	$ 1,950	$ 1,950	$ 1,950
Price increases	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Mean Number of injections/year	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
Eylea, per vial	$ 1,850	$ 1,850	$ 1,850	$ 1,850	$ 1,850	$ 1,850	$ 1,850	$ 1,850
Price increases	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Mean Number of injections/year	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0
Fovista, per vial	$ 1,400	$ 1,400	$ 1,400	$ 1,400	$ 1,400	$ 1,400	$ 1,400	$ 1,400
Price increases	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Mean Number of injections/year	6.5	7.0	6.7	6.5	6.3	6.3	6.3	6.3
Summary of Product Revenues	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**
Avastin summary								
Avastin patients	123	123	123	126	127	129	130	132
Avastin annual cost	$ 496	$ 496	$ 496	$ 496	$ 496	$ 496	$ 496	$ 496
Avastin revenues ($, M)	**61**	**61**	**61**	**63**	**63**	**64**	**65**	**65**
Y/Y Growth (%)	*5%*	*0%*	*0%*	*2%*	*1%*	*1%*	*1%*	*1%*
Lucentis summary								
Lucentis patients	71	69	68	68	68	67	66	66
Lucentis annual cost	$ 15,600	$ 15,600	$ 15,600	$ 15,600	$ 15,600	$ 15,600	$ 15,600	$ 15,600
Lucentis revenues ($, M)	**1,102**	**1,077**	**1,058**	**1,062**	**1,054**	**1,045**	**1,036**	**1,026**
Y/Y Growth (%)	*0%*	*-2%*	*-2%*	*0%*	*-1%*	*-1%*	*-1%*	*-1%*
Eylea summary								
Eylea patients	114	115	117	121	124	126	129	132
Eylea annual cost	$ 12,950	$ 12,950	$ 12,950	$ 12,950	$ 12,950	$ 12,950	$ 12,950	$ 12,950
Eylea revenues ($, M)	**1,471**	**1,490**	**1,518**	**1,568**	**1,601**	**1,635**	**1,670**	**1,703**
Y/Y Growth (%)	*6%*	*1%*	*2%*	*3%*	*2%*	*2%*	*2%*	*2%*
Fovista summary								
Fovista patients	21	43	58	76	90	101	102	103
Fovista annual cost	$ 9,100	$ 9,800	$ 9,380	$ 9,100	$ 8,750	$ 8,750	$ 8,750	$ 8,750
Fovista revenues ($, M)	**188**	**425**	**548**	**687**	**784**	**881**	**890**	**899**
Y/Y Growth (%)		*126%*	*29%*	*25%*	*14%*	*12%*	*1%*	*1%*
Total US AMD Market	2,822	3,053	3,185	3,380	3,503	3,625	3,660	3,694

Source: J.P. Morgan estimates.

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Table 11: AMD EU Market Model (2012- 24E)

Wet AMD EU Market Model	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Diagnosed Prevalence of Adv. AMD, EU	2,760	2,780	2,800	2,820	2,837	2,855	2,872	2,890
% pts wet AMD	12%	12%	12%	12%	12%	12%	12%	12%
% with bilateral disease	40%	40%	40%	40%	40%	40%	40%	40%
Addr. Pop - Eyes with wAMD	464	467	470	474	477	480	483	486
Treatment Paradigm Structure								
% Treated with anti-VEGF monotherapy	90%	87%	82%	74%	69%	66%	64%	63%
% Treated with combo (anti-VEGF + anti-PDGF)	0%	4%	10%	18%	23%	26%	28%	29%
% Treated with anti-PDGF monotherapy	0%	0%	0%	0%	0%	0%	0%	0%
% Treated	90%	91%	91.6%	92.0%	92.0%	92.0%	92.0%	92.0%
% Treated with anti-PDGF	0%	4%	10%	18%	23%	26%	28%	29%
VEGF Market Share	90.5%	90.5%	91.6%	92.0%	92.0%	92.0%	92.0%	92.0%
Avastin	20%	20%	20%	20%	20%	20%	20%	20%
Lucentis	48%	44%	40%	38%	36%	35%	35%	35%
Eylea	32%	36%	40%	42%	44%	45%	45%	45%
Patients on Therapy								
Total treated patients	**420**	**423**	**431**	**436**	**439**	**441**	**444**	**447**
Fovista	0	16	47	85	110	125	135	141
VEGF Treated	420	423	431	436	439	441	444	447
Avastin	84	85	86	87	88	88	89	89
Lucentis	201	186	172	166	158	154	155	156
Eylea	134	152	172	183	193	199	200	201
Pricing Analysis (USD)								
Avastin, per vial	$ 166	$ 165	$ 163	$ 161	$ 160	$ 158	$ 157	$ 155
Price increases	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*
Mean Number of injections/year	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5
Lucentis, per vial	$ 1,099	$ 1,088	$ 1,077	$ 1,067	$ 1,056	$ 1,045	$ 1,035	$ 1,025
Price increases	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*
Mean Number of injections/year	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
Eylea, per vial	$ 1,122	$ 1,110	$ 1,099	$ 1,088	$ 1,077	$ 1,067	$ 1,056	$ 1,045
Price increases	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*
Mean Number of injections/year	7.0	7.0	7.0	7.0	7.0	7.0	7.0	7.0
Fovista, per vial	$ 1,000	$ 1,000	$ 1,000	$ 990	$ 980	$ 970	$ 961	$ 951
Price increases	*0%*	*0%*	*0%*	*-1%*	*-1%*	*-1%*	*-1%*	*-1%*
Mean Number of injections/year	6.7	6.7	6.6	6.5	6.3	6.3	6.3	6.3

Summary of Product Revenues	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Avastin summary								
Avastin patients	84	85	86	87	88	88	89	89
Avastin annual cost	$ 1,410	$ 1,396	$ 1,382	$ 1,368	$ 1,355	$ 1,341	$ 1,328	$ 1,315
Avastin revenues ($, M)	**118**	**118**	**119**	**119**	**119**	**118**	**118**	**117**
Y/Y Growth (%)	*1%*	*0%*	*1%*	*0%*	*0%*	*0%*	*0%*	*0%*
Lucentis summary								
Lucentis patients	201	186	172	166	158	154	155	156
Lucentis annual cost	$ 8,795	$ 8,707	$ 8,620	$ 8,534	$ 8,448	$ 8,364	$ 8,280	$ 8,197
Lucentis revenues ($, M)	**1,771**	**1,619**	**1,486**	**1,413**	**1,334**	**1,292**	**1,287**	**1,282**
Y/Y Growth (%)	*-7%*	*-9%*	*-8%*	*-5%*	*-6%*	*-3%*	*0%*	*0%*
Eylea summary								
Eylea patients	134	152	172	183	193	199	200	201
Eylea annual cost	$ 7,852	$ 7,773	$ 7,695	$ 7,618	$ 7,542	$ 7,467	$ 7,392	$ 7,318
Eylea revenues ($, M)	**1,054**	**1,183**	**1,326**	**1,395**	**1,455**	**1,483**	**1,477**	**1,471**
Y/Y Growth (%)	*14%*	*12%*	*12%*	*5%*	*4%*	*2%*	*0%*	*0%*
Fovista summary								
Fovista patients	0	16	47	85	110	125	135	141
Fovista annual cost	$ 6,700	$ 6,650	$ 6,620	$ 6,435	$ 6,126	$ 6,064	$ 6,004	$ 5,944
Fovista revenues ($, M)	**-**	**109**	**311**	**549**	**672**	**756**	**811**	**837**
Y/Y Growth (%)			*186%*	*76%*	*22%*	*13%*	*7%*	*3%*
Total EU AMD Market	2,944	3,028	3,242	3,476	3,579	3,649	3,692	3,707

Source: J.P. Morgan estimates.

Manufacturing

Ophthotech relies on third-party manufacturers to produce lots of Fovista. Additionally, a key component involved in the production of Fovista is a proprietary polyethylene glycol, or PEG, reagent accessed under a supply agreement with Nektar. As such, Ophthotech is contractually obligated to pay Nektar up to $5.5M in clinical and regulatory milestones, $3M in commercial milestones, as well as a double-digit percentage of any upfront or milestone payments should Ophthotech sublicense the drug in any or all territories.

Intellectual Property

Ophthotech holds patents covering the composition of matter of Fovista that, barring any Hatch-Waxman extension, are set to expire by YE17 (see Table 12). Factoring in the full 5-year extension would leave the drug protected through YE22. The company also had use patents protecting the use of combination therapy (i.e., Fovista plus Lucentis or Avastin) in patients with wet AMD. That patent is not set to expire until 2024. The company has also filed patent applications protecting combination use with Eylea, potentially through 2030. Though use patents are more difficult to defend, we have, nevertheless, modeled sales for Fovista in our models out through 2024. Even though the composition of matter patent will have expired by then, we believe the drug's complex manufacturing and use of a proprietary PEG moiety should create meaningful hurdles to a generic entrant entering the market.

Table 12: Selected Fovista Patents

Patent #	Patent Title	Expiry
6,229,002	Platelet-derived growth factor (PDGF) nucleic acid ligand complexes *Composition of Matter*	US: Dec, 16, 2017 EU & JPN: 2018
7,759,472	Combination therapy for the treatment of ocular neovascular disorders	US & EU: Aug 26, 2024

Source: USPTO, J.P. Morgan Analysis

ARC1905 for Wet AMD

ARC1905 is a chemically synthesized pegylated aptamer designed to inhibit complement factor C5. The complement system represents a series of proteins produced in the liver that play a key role in eradicating foreign pathogens. Inhibiting complement factor C5 prevents the formation of the key terminal fragments, C5a and C5b-9, with relative sparing of immunoprotective functions. C5a is an inflammatory activator, and C5b-9 induces cell death. There is a growing body of evidence implicating the A complement-mediated inflammatory component in AMD.

Clinical Development

Ophthotech previously ran an ascending dose (0.3 mg, 1.0 mg or 2.0 mg), open-label phase 1/2a study evaluating the safety and tolerability of ARC1905 in combination with Lucentis for the treatment of wet AMD. The combination was reasonably well tolerated with only a single adverse event: a mild subcapsular cataract. In a subgroup of 43 patients who had not previously been treated with anti-VEGF therapy and who

received six injections at doses of ARC1905 in combination with Lucentis, there was a clear trend toward a mean increase in visual acuity from baseline at all timepoints. At a follow-up visit at week 24 of the trial, there was an improvement in mean visual acuity from baseline of 13.6 letters for the 0.3 mg dose group, 11.7 letters for the 1.0 mg dose group and 15.3 letters for the 2.0 mg dose group. In this subgroup, 22 patients (51%) gained at least 15 letters, 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.

Based on the Ophthotech S-1 filing, the company expects to focus its development efforts for ARC1905 on a subpopulation of patients with wet AMD who do not respond adequately to treatment with anti-VEGF monotherapy and are defined as anti-VEGF resistant on the basis of complement-mediated inflammation. As such, we expect the company to initiate a clinical trial in 2014 with ARC1905 in combination with an anti-VEGF drug for the treatment of wet AMD patients who have experienced anti-VEGF treatment failure and are defined as anti-VEGF resistant on the basis of complement-mediated inflammation. The study is expected to enroll up to 50 patients with data expected in 2015.

Market Projections

We currently do not include any revenues for ARC1905 in our model, nor do we include it in our valuation. We await further data from the planned ARC1905 trial, and further scientific evidence supporting the role of complement in treating wet AMD.

Intellectual Property

Archemix holds a composition of matter patent for ARC1905 that extends until 2025 for the US and EU. Additionally, Archemix also holds use patents covering the treatment of certain complement protein mediated disorders with ARC1905, and these are expected to expire in 2026.

Financial Outlook

Income Statement

We project the company will begin generating revenues in FY17 ($188M), growing to $533M in FY18. As such, we anticipate expect the company to turn profitable in FY17 – the same year Fovista will launch in the US. We expect the company to burn roughly $220M (in line with company guidance of $225M) between the end of 2Q13 and the start of 3Q16, around the read-out of data. Longer term we forecast gross margins of ~80%, accounting for royalty streams owed to Astellas, Novo A/S, and the cost of manufacturing (Table 14). We forecast FY13-18 EPS results of ($3.48), ($2.07), ($2.26), ($2.72), $0.20 and $6.00, respectively. Our estimates based on a current share count of ~31.3 million (exclusive of ~2.6 million stock options outstanding). We forecast future share counts based on a modest rate of stock options being exercised, a 2 million share offering in FY16, and the company becoming profitable in FY17 (see Table 16).

Balance Sheet and Cash Flow

As of the completion of the IPO, OPHT had roughly $230M in cash, cash equivalents, and marketable securities. Additionally, the company has two existing tranches of $83M it can draw down from its royalty purchase agreement with Novo A/S. We believe the company has adequate resources to last until 2017. However, we expect the company will raise additional funds ahead of the read-out of the pivotal Fovista studies. Our projected balance sheet and cash flow statement are detailed in Table 16 and Table 17.

Novo A/S Financing

In May 2013, Ophthotech entered in a royalty purchase arrangement with the venture capital arm, Novo A/S, of Novo Nordisk (covered by JPM analyst Richard Vosser). In exchange for potential financing of up to $125M, Ophthotech sold Novo A/S a royalty interest on worldwide sales of Fovista. Ophthotech received the first tranche ($41.7M) immediately upon closing of the agreement in exchange for a low-single-digit royalty on Fovista sales. For the sake of our models we assume Ophthotech will draw down on the remaining $83M and will ultimately owe Novo A/S a royalty of ~6% of Fovista sales (vs. company guidance of a "low- to mid-single-digit" royalty). The closing of the two subsequent tranches is subject to undisclosed enrollment milestones in the phase 3 pivotal trials for the drug.

Valuation

Our December 2014 price target of $40 for OPHT is based on our sum-of-the-parts NPV analysis. In order to complete our analysis, we projected sales of Fovista from a launch in 2017 through 2025. We assume a 12.5% WACC, and conservatively modeled in zero terminal values for the drug in the US and EU.

Based on the projections and assumptions detailed above, as well as probability adjustments for Fovista, we derive a valuation of $40/share (detailed below, Table 13) comprising US sales of Fovista of $21/sh, OUS sales of Fovista of $14/sh, and $5/sh for net cash. Our probability adjustment (80%) for Fovista is in line with our typical practice in that assets with successful phase 2 studies are typically probability adjusted between 75% and 85%. Given the robustness of the Phase 2 data set, we view our 80% probability adjustment as appropriate.

Table 13: Sum-of-the-Parts Valuation

	Total	Value/Share
Fovista - AMD ($ in millions)	**1,227**	**$35**
US	745	$21
EU	481	$14
Net Cash ($ in millions) at YE13	**184**	**$5**
Total ($ in millions)	**1,410**	**$40**

Source: J.P. Morgan estimates.

Table 14: Contractually Obligated Milestones and Royalties Related to Fovista and ARC1005

Company	Drug	Milestones	Royalties[1]
Archemix	Fovista	$16.5M in clinical and regulatory milestones, including $2MM due upon initiation of Ph 3 trial. $2M paid through June 30, 2013 $3M in commercial milestones	None
Astellas	Fovista	$12M in aggregate upon US/EU approval	"Low- to mid-single-digit" royalties[1]
Nektar	Fovista	$5.5 in clinical and regulatory milestones, including $1MM due upon initiation of Ph 3 trials. $750k paid through June 30, 2013 $3M in commercial milestones Low "Double-digit" percentage of upfront payment related to sub-licensing Fovista and a "higher double-digit percentage" on milestones payment	None
Novo A/S	Fovista	None	"Low- to mid-single-digit" royalties[2]
Archemix	ARC1005	$57.5M in development, clinical, and regulatory milestones $22.5M in commercial milestones "Double-digit" percentage of any non-royalty payment Ophthotech receives from sub-licensing ARC1905	None

[1] On net sales [2] Assumes all tranches are drawn down

Source: Company reports and J.P. Morgan estimates.

Management

David Guyer, M.D. – Chief Executive Officer

David Guyer, M.D., is a co-founder and chief executive officer of Ophthotech Corporation, while also serving as chairman of its board of directors. Dr. Guyer previously worked as a venture capitalist and partner at SV Life Sciences. Prior to joining SV Life Sciences, Dr. Guyer co-founded and served as CEO and director at Eyetech Pharmaceuticals, Inc., at which he oversaw the development and commercialization of Macugen (pegaptanib sodium), the first FDA-approved anti-VEGF pharmacological treatment for wet AMD. Prior to starting Macugen, he was the professor and chairman of the Department of Ophthalmology at New York University School of Medicine. Dr. Guyer received his Bachelor of Science (B.S.) degree from Yale College summa cum laude and his medical degree (M.D.) from Johns Hopkins Medical School. He completed his ophthalmology residency at Wilmer Ophthalmological Institute at Johns Hopkins Hospital and a retinal fellowship at the Massachusetts Eye and Ear Infirmary at Harvard Medical School.

Samir Patel, M.D. – President

Samir Patel, M.D. is a co-founder and president of Ophthotech Corporation. He also serves as vice chairman of its board of directors. Previously, Dr. Patel was the co-founder of Eyetech Pharmaceuticals, Inc., at which he was the chief medical officer and served on its board of directors. Prior to joining Ophthotech, Dr. Patel served as the director of the Retina Service and the residency program as well as an associate professor of Ophthalmology at the University of Chicago, Department of Ophthalmology and Visual Science. His academic research focused on cell-based therapies for age-related macular degeneration. Dr. Patel received his medical degree (M.D.) from the University of Massachusetts Medical School and ophthalmology training from the University of Chicago. He received his training in retinal surgery from the Massachusetts Eye and Ear Infirmary at Harvard Medical School.

Bruce Peacock – Chief Financial and Business Officer

Bruce Peacock is the chief financial and business officer of Ophthotech Corporation. Prior to Ophthotech, Mr. Peacock was the CEO of Alba Therapeutics. He has served as CEO of The Little Clinic, Adolor Corporation and Orthovita, Inc. and has also held senior management positions at Cephalon, Inc. and Centocor, Inc. Mr. Peacock currently serves as a venture partner with SV Life Sciences Advisors, LLC., is co-chairman of Alba Therapeutics, and is a director of Discovery Labs and Invisible Sentinel, Inc. Mr. Peacock holds a Bachelor of Arts (B.A.) degree from Villanova University and is a Certified Public Accountant.

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Financial Statements

Table 15: OPHT Income Statements (2012A - 2018E)

Dollars in millions except per share data
Fiscal year ended December 31

	2012A	1Q13A	2Q13A	3Q13E	4Q13E	2013E	1Q14E	2Q14E	3Q13E	4Q13E	2014E	2015E	2016E	2017E	2018E
Revenues															
US Fovista	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	188.2	425.1
OUS Fovista	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	108.7
Total Revenues	**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**	**188.2**	**533.8**
Operating Expenses															
Cost of sales	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	37.6	85.0
Research and development	6.8	3.4	3.4	11.5	9.5	27.7	10.8	11.6	12.2	12.5	47.1	58.9	76.6	88.1	96.0
Sales, general and administrative	6.9	2.5	2.5	4.8	4.0	13.8	4.0	4.1	4.1	4.2	16.4	17.7	24.8	55.3	66.3
Total Operating expenses	**13.7**	**5.9**	**5.9**	**16.3**	**13.5**	**41.5**	**14.8**	**15.7**	**16.3**	**16.7**	**63.5**	**76.6**	**101.4**	**181.0**	**247.4**
Operating Income	**(13.7)**	**(5.9)**	**(5.9)**	**(16.3)**	**(13.5)**	**(41.5)**	**(14.8)**	**(15.7)**	**(16.3)**	**(16.7)**	**(63.5)**	**(76.6)**	**(101.4)**	**7.2**	**286.4**
Interest income, net	(0.5)	(0.7)	(0.7)	(0.7)	(0.7)	(2.9)	(0.7)	(0.7)	(0.7)	(0.7)	(2.8)	1.0	2.0	1.0	3.0
Other income, net	(0.4)	(0.7)	(0.7)	0.0	0.0	(1.5)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Other Income	(0.9)	(1.5)	(1.5)	(0.7)	(0.7)	(4.3)	(0.7)	(0.7)	(0.7)	(0.7)	(2.8)	1.0	2.0	1.0	3.0
Pretax Income	(14.6)	(7.3)	(7.3)	(17.0)	(14.2)	(45.8)	(15.5)	(16.4)	(17.0)	(17.4)	(66.3)	(75.6)	(99.4)	8.2	289.4
Income tax (benefit)	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	43.4
Net Income	(14.6)	(7.3)	(7.3)	(17.0)	(14.2)	(45.8)	(15.5)	(16.4)	(17.0)	(17.4)	(66.3)	(75.6)	(99.4)	8.2	246.0
Accretion of preffered stock dividends	(7.1)	(1.8)	(1.8)	(1.8)		(5.4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income allocable to common stockholders	(21.6)	(9.1)	(9.1)	(18.8)	(14.2)	(51.2)	(15.5)	(16.4)	(17.0)	(17.4)	(66.3)	(75.6)	(99.4)	8.2	246.0
Diluted GAAP EPS	**(2.52)**	**(1.05)**	**(1.05)**	**(1.84)**	**(0.45)**	**(3.48)**	**(0.49)**	**(0.51)**	**(0.53)**	**(0.54)**	**(2.07)**	**(2.26)**	**(2.72)**	**0.20**	**6.00**
Fully diluted shares outstanding	8.6	8.7	8.7	10.2	31.3	14.7	31.7	32.0	32.3	32.5	32.1	33.5	36.5	40.0	41.0

Source: Company reports and J.P. Morgan estimates.

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Table 16: OPHT Balance Sheet

Dollars in millions Fiscal year ended December 31	2011A	2012A	2013E	2014E	2015E	2016E
	FY	FY	FY	FY	FY	FY
Assets						
Cash and cash equivalents	6.40	4.30	169.75	145.07	111.09	76.79
Prepaid expenses and other current assets	0.06	0.04	0.04	0.04	0.04	0.04
Other recievables	1.04	-			-	-
Debt issuance costs	-	0.33	0.33	0.33	0.33	0.33
Security deposits	-	0.16	0.16	0.16	0.16	0.16
Total Current Assets	**7.50**	**4.84**	**170.28**	**145.60**	**111.63**	**77.32**
PP&E, net	0.07	0.04	0.04	0.04	0.04	0.04
Security deposits	0.16	-	-	-	-	-
Total Long Term Assets	**0.23**	**0.04**	**0.04**	**0.04**	**0.04**	**0.04**
Total Assets	**7.73**	**4.88**	**170.32**	**145.65**	**111.67**	**77.36**
Liabilities and Equity						
Notes payable	-	11.04	11.04	11.04	11.04	11.04
Accrued clinical drug supplies and tiral costs	1.50	1.01	1.01	1.01	1.01	1.01
Accounts payable and accrued expenses	0.85	0.87	0.87	0.87	0.87	0.87
Accrued bonuses	0.78	0.53	0.53	0.53	0.53	0.53
Warrant liability	0.19	0.97	0.97	0.97	0.97	0.97
Deferred revenue	0.02	-	-	-	-	-
Total Current Liabilities	**3.34**	**14.41**	**14.41**	**14.41**	**14.41**	**14.41**
Prefered stock	106.88	113.94	113.94	113.94	113.94	113.94
Total Liabilities	**110.22**	**128.35**	**128.35**	**128.35**	**128.35**	**128.35**
Junior Series A convertible preferred	3.00	3.00	3.00	3.00	3.00	3.00
Common stock	0.01	0.01	0.01	0.01	0.01	0.01
Deficit accumulated during development stage	(105.50)	(126.48)	38.96	14.29	(19.69)	(53.99)
Total Shareholders' Equity	**(102.49)**	**(123.47)**	**41.97**	**17.30**	**(16.68)**	**(50.99)**
Total Liabilities and Equity	**7.73**	**4.88**	**170.32**	**145.65**	**111.67**	**77.36**

Source: Company reports and J.P. Morgan estimates.

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Table 17: OPHT Statement of Cash Flows

Dollars in millions Fiscal year ended December 31	2011A	2012A	2013E	2014E	2015E	2016E
	FY	FY	FY	FY	FY	FY
Net Income	(18.63)	(14.56)	(51.22)	(66.34)	(75.64)	(99.41)
Depreciation	0.03	0.03	0.03	0.03	0.03	0.03
Ammortization of debt issuance costs	-	0.05				
Accretion of debt discount	-	0.06				
Non-Cash change in fari value of warrant liability	0.01	0.37				
Stock-based compensation expense	0.25	0.64				
Stock issued	0.50	-				
Changes in operating assets and liabilites:						
Prepaid expenses and other	0.14	0.02	-	-	-	-
Other receivables	(0.74)	1.04				-
Security deposits	(0.00)	(0.00)	-	-	-	-
Accrued clinical drug supplies and trial costs	(0.82)	(0.48)	-	-	-	-
Accounts payable and accrued expenses	(0.05)	0.01	-	-	-	-
Accrued bonusses	0.22	(0.25)	-	-	-	-
Deferred rent	(0.02)	(0.02)	-	-	-	-
Net change in Working Capital	(1.28)	0.32	-	-	-	-
Net Cash From Operations	**(19.12)**	**(13.10)**	**(51.19)**	**(66.31)**	**(75.61)**	**(99.38)**
Purchase of marketable securities	-	-	-	-	-	-
Maturities of marketable securities	3.40	-	-	-	-	-
Purchase of property plant and equipment	(0.00)	-	(0.03)	(0.03)	(0.03)	(0.03)
Net Cash from Investing	**3.40**	**-**	**(0.03)**	**(0.03)**	**(0.03)**	**(0.03)**
Debt issuance costs	-	(0.38)				
Proceeds from Issuance of common stock	0.00	0.00	175.00			65.10
Proceeds from royalty purchase agreement			41.67	41.67	41.67	
Proceeds from issuance of notes payable, net	-	11.39				
Proceeds form issuance of preferred stock, net	14.99	-				
Net Cash from Financing	**14.99**	**11.01**	**216.67**	**41.67**	**41.67**	**65.10**
Net Increase (Decrease) in Cash	**(0.73)**	**(2.09)**	**165.44**	**(24.68)**	**(33.98)**	**(34.31)**
Cash and cash equivalents at BOP	**7.13**	**6.40**	**4.30**	**169.75**	**145.07**	**111.09**
Cash and cash equivalents at EOP	**6.40**	**4.30**	**169.75**	**145.07**	**111.09**	**76.79**

Source: Company reports and J.P. Morgan estimates.

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Ophthotech: Summary of Financials

Income Statement - Annual	FY12A	FY13E	FY14E	FY15E	Income Statement - Quarterly	1Q13A	2Q13A	3Q13E	4Q13E
Revenues	0	0	0	0	Revenues	0A	0A	0	0
Cost of products sold	0	0	0	0	Cost of products sold	0A	0A	0	0
Gross profit	-	-	-	-	Gross profit	-	-	-	-
SG&A	(7)	(14)	(16)	(18)	SG&A	(2)A	(2)A	(5)	(4)
R&D	(7)	(28)	(47)	(59)	R&D	(3)A	(3)A	(12)	(10)
Operating income	(14)	(42)	(64)	(77)	Operating income	(6)A	(6)A	(16)	(14)
EBITDA	(14)	(42)	(64)	(77)	EBITDA	(6)A	(6)A	(16)	(14)
Net interest (income) / expense	-	-	-	-	Net interest (income) / expense	-	-	-	-
Other income / (expense)	(1)	(4)	(3)	1	Other income / (expense)	(1)A	(1)A	(1)	(1)
Income taxes	0	0	0	0	Income taxes	0A	0A	0	0
Net income - GAAP	(22)	(51)	(66)	(76)	Net income - GAAP	(9)A	(9)A	(19)	(14)
Net income - recurring	(22)	(51)	(66)	(76)	Net income - recurring	(9)A	(9)A	(19)	(14)
Diluted shares outstanding	9	15	32	34	Diluted shares outstanding	9A	9A	10	31
EPS - excluding non-recurring	(2.52)	(3.48)	(2.07)	(2.26)	EPS - excluding non-recurring	(1.05)A	(1.05)A	(1.84)	(0.45)
EPS - recurring	(2.52)	(3.48)	(2.07)	(2.26)	EPS - recurring	(1.05)A	(1.05)A	(1.84)	(0.45)
Balance Sheet and Cash Flow Data	**FY12A**	**FY13E**	**FY14E**	**FY15E**	**Ratio Analysis**	**FY12A**	**FY13E**	**FY14E**	**FY15E**
Cash and cash equivalents	4	170	145	111	Sales growth	-	-	-	-
Accounts receivable	0	0	0	0	EBIT growth	-	203.4%	53.1%	20.6%
Inventories	-	-	-	-	EPS growth - recurring	-	38.1%	(40.7%)	9.3%
Other current assets	0	0	0	0					
Current assets	5	170	146	112	Gross margin	-	-	-	-
PP&E	0	0	0	0	EBIT margin	-	-	-	-
Total assets	5	170	146	112	EBITDA margin	-	-	-	-
					Tax rate	0.0%	0.0%	0.0%	0.0%
Total debt	11	11	11	11	Net margin	-	-	-	-
Total liabilities	128	128	128	128					
Shareholders' equity	(123)	42	17	(17)	Net Debt / EBITDA	(49.2%)	382.3%	210.9%	130.5%
					Net Debt / Capital (book)	(5.8%)	136.0%	114.8%	85.7%
Net income (including charges)	(15)	(51)	(66)	(76)					
D&A	0	0	0	0	Return on assets (ROA)	(886.3%)	(58.5%)	(42.0%)	(58.8%)
Change in working capital	0	0	0	0	Return on equity (ROE)	35.0%	125.7%	(223.9%)	(24589.3%)
Other	1	0	0	0					
Cash flow from operations	(13)	(51)	(66)	(76)	Enterprise value / sales	-	-	-	-
					Enterprise value / EBITDA	-	-	-	-
Capex	0	(0)	(0)	(0)	Free cash flow yield	(5.2%)	(11.9%)	(7.1%)	(7.7%)
Free cash flow	(13)	(51)	(66)	(76)					
Cash flow from investing activities	0	(0)	(0)	(0)					
Cash flow from financing activities	11	217	42	42					
Dividends	-	-	-	-					
Dividend yield	-	-	-	-					

Source: Company reports and J.P. Morgan estimates.
Note: $ in millions (except per-share data).Fiscal year ends Dec

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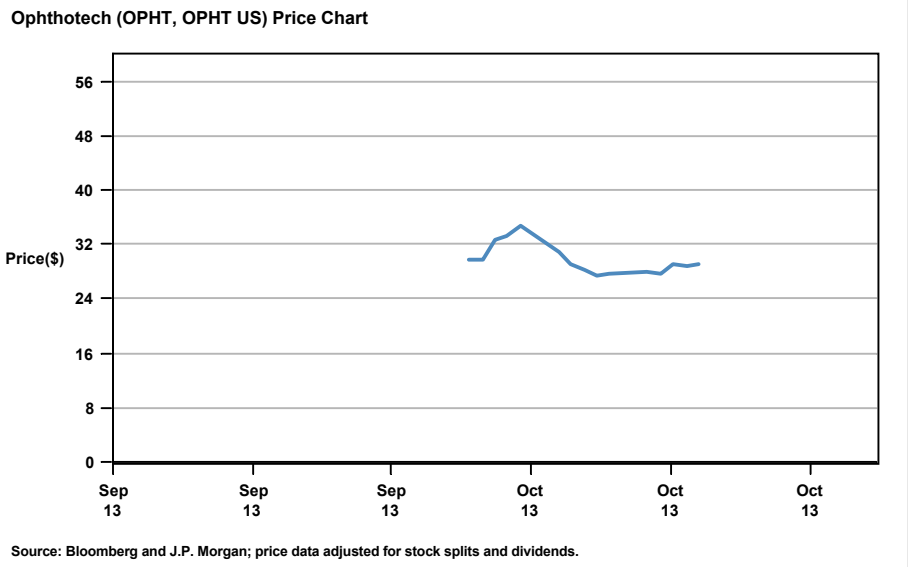

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IB clients*	76%	65%	57%

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