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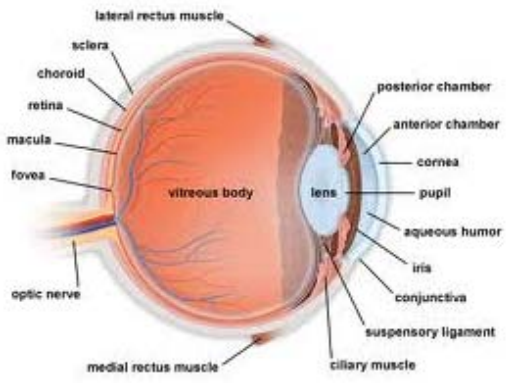
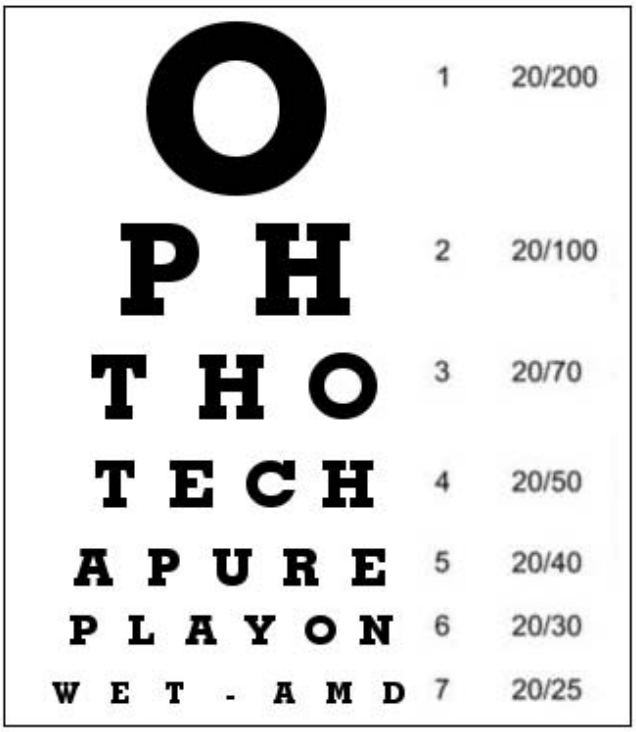
AGE-RELATED MACULAR DEGENERATION



Source: www.centralillinoisvision.com



Ophthotech Corp. (OPHT - $40.00 - NASDAQ)

Kevin Kedra
(914) 921-7721

-Please Refer To Important Disclosures On Page 13 Of This Report-

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Ophthotech Corp. (OPHT - $40.00 - NASDAQ) Eye Care Biotech Rises Again - Buy

Year	EPS [(a)]	PMV	
2016P	($4.25)	$87	Dividend: None Current Return: Nil
2015P	(2.70)	80	Shares O/S: 33.3 million
2014E	3.60	73	52-Week Range: $47.99 – $22.61
2013A	(6.34)	--	

(a) Adjusted EPS excluding certain amortization charges, milestone payments, and other one-time charges

COMPANY OVERVIEW

Ophthotech, located in New York, NY, is a clinical stage biotechnology company focused on treating diseases of the back of the eye. The company's two lead compounds are Fovista, a PDGF-inhibitor in Phase III for wet age-related macular degeneration (wet AMD), and Zimura, a C5-inhibitor in Phase II for dry AMD. OPHT went public in September 2013 at an IPO price of $22 per share.

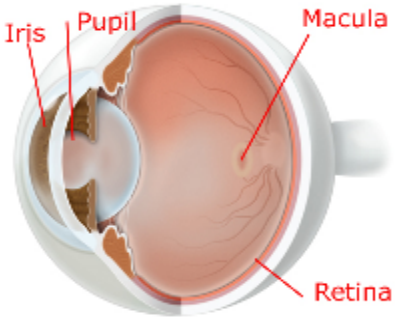
- *Large, fast-growing market opportunity.* AMD is the leading cause of blindness in the US. The global market for drugs approved for wet AMD was approximately $6.2 billion in 2013 and has grown at a 26% annual rate over the past five years. As a combination therapy with anti-VEGF drugs (current standard of care), Fovista could significantly expand the wet AMD market. We estimate that Fovista sales could reach $1.2 billion in the US and $1.8 billion globally by 2020.
- *Established proof-of-concept.* Fovista is currently in Phase III studies after demonstrating proof-of-concept in Phase II. Fovista + Lucentis showed a statistically significant 62% benefit in visual acuity (VA) improvement vs. Lucentis monotherapy at 24 weeks in wet AMD patients. This is the first time a drug has demonstrated superiority to the current standard of care, and Ophthotech believes that the one-year Phase III data could show an even stronger efficacy signal based on continued improvements over time throughout the Phase II study.
- *2-3 year lead time on competitors*. Ophthotech expects to have Phase III Fovista data and file for approval by the end of 2016, which could lead to a 2017 approval. The nearest competitors are in Phase I or early Phase II development. We would not expect another non-VEGF competitor in wet AMD to reach the market prior to 2020, giving Fovista at least a 2-3 year lead time.
- *Novartis deal validates technology*. In May 2014, Ophthotech and Novartis, who markets Lucentis ex-US, reached a licensing agreement for ex-US rights to Fovista. Ophthotech received $200 million upfront and is eligible for up to $830 million in milestones and a mid-30% royalty. This deal provides OPHT with an established international partner and cash to help finance the company until profitability with Fovista.
- *Experienced management*. Co-founders Dr. David Guyer (CEO, Chairman) and Dr. Samir Patel (President, Vice Chairman) were also the co-founders of Eyetech Pharmaceuticals, where they developed Macugen, the first approved anti-VEGF therapy for wet AMD. After selling Eyetech to OSI Pharmaceuticals in November 2005 for $935 million, the two formed Ophthotech and bought back the rights to OSI/Eyetech's preclinical anti-PDGF assets, including Fovista, for $4 million plus stock, milestones, and royalties in 2007.
- *Zimura for dry AMD*. Zimura is currently in Phase II for geographic atrophy (GA), an advance form of dry AMD. While dry AMD accounts for 85-90% of the estimated 30 million people worldwide with AMD, there are currently no approved treatments. Ophthotech plans to initiate a Phase 2/3 study with results expected in 2016. Our estimates and valuation exclude any benefit from Zimura, so positive proof-of-concept results would add further upside to our OPHT investment thesis.
- *Initiating with Buy*. We are initiating coverage on Ophthotech with a Buy recommendation. We believe that Fovista will be the next blockbuster wet AMD drug and is one of the most attractive non-cancer assets in biotech. By 2020, we expect Fovista sales to reach $1.2 billion in the US and $1.8 billion globally, resulting in EBITDA of $725 million and EPS of $12.15 per share. OPHT currently trades at a 50% discount to our 2015 PMV of $80 per share.

THE ABC'S OF AMD

What is AMD?

Age-related macular degeneration (AMD) is the leading cause of blindness in people age 50 and older in both the US and European Union. Worldwide, the disease is the third-leading cause of blindness, behind cataracts and glaucoma. AMD results from damage to the macula, a small area near the center of the retina that is essential for central vision. AMD is a progressive disease that gets worse over time due to a buildup of yellow deposits beneath the retina called drusen. As the disease progresses, damage to the macula becomes more severe, resulting in blurry, distorted, or dark central vision that can ultimately progress to blindness. Patients may experience AMD in one or both eyes, and the disease's stage of development can differ from one eye to the other.

Exhibit 1 Human Eye



Source: www.enhancedvision.com

Wet AMD vs. Dry AMD

Patients with early and intermediate stages of AMD will have some drusen and loss of retinal pigmentation, but most will not experience major symptoms of vision loss until progressing to late stage AMD. There are two types of late stage AMD – wet AMD and dry AMD.

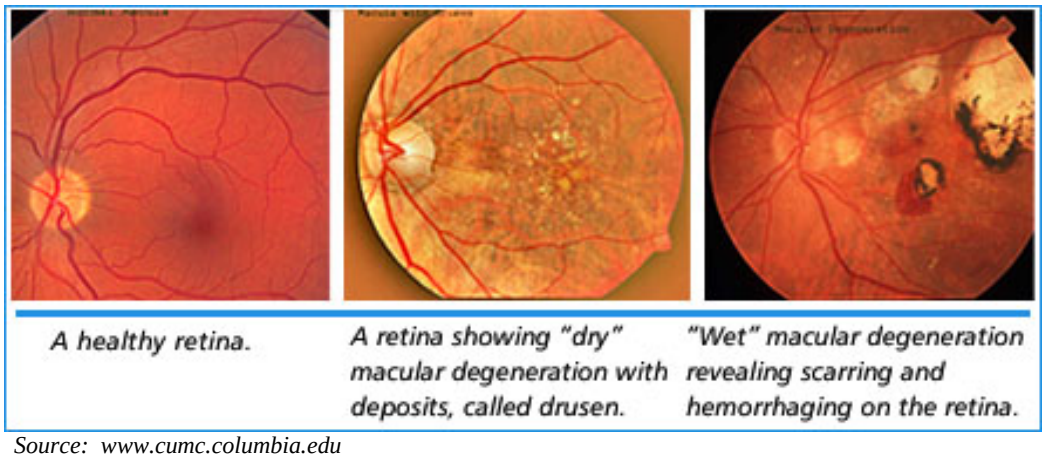
Exhibit 2 Effects of AMD

Source: www.gene.com

Dry AMD, also called geographic atrophy, occurs due to the gradual breakdown of light-sensitive cells in the macula as well as the supportive tissue beneath the retina. The disease is typically associated with drusen buildup and is the more gradual of the two types. An estimated 85-90% of late-stage patients have dry AMD.

Wet AMD, also called neovascular AMD, is caused by abnormal blood vessel growth beneath the retina. These vessels can leak blood and fluid, resulting in swelling and additional damage to the retina. Progression from the dry form to the wet form of AMD often leads to rapid disease progression and vision loss. Despite only affecting 10-15% of late-stage patients, wet AMD accounts for 80-90% of cases of blindness caused by the disease.

Exhibit 3 Dry vs. Wet AMD



Source: www.cumc.columbia.edu

Who has AMD?

According to estimates from the National Institute of Health (NIH), approximately 10-15 million Americans suffer from some form of AMD, with over 2 million suffering from late stage AMD. Americans account for approximately one-third of the 30-50 million patients worldwide with AMD. Age is the biggest risk factor for the disease. AMD is most commonly found in people over the age of 50 and increases in both prevalence and severity with age. The NIH estimates that the rate of late stage AMD increases from 1% of the population aged 65 to nearly 12% of the population aged 80+. Women are at higher risk of AMD than men, though this may be partly due to longer average life spans. Caucasians have an estimated 2-3x increased risk of developing late stage AMD compared to blacks and Hispanics. Other factors that increase the risk of AMD are smoking, obesity, and genetic predisposition. Each year, approximately 200,000 new cases of wet AMD are diagnosed in US and 600,000 new cases are diagnosed worldwide.

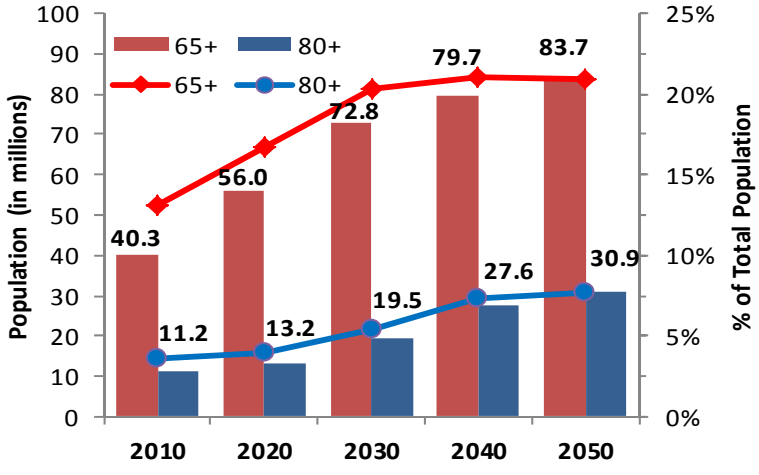
Exhibit 4 **Prevalence of Late Stage AMD by Age (50+) in US 2010**

Age Group	Prevalence Rate
50 – 54	0.36%
55 – 59	0.41
60 – 64	0.57
65 – 69	0.91
70 – 75	1.63
75 – 79	3.16
80+	11.73
Total	**2.09%**

Source: National Eye Institute of NIH

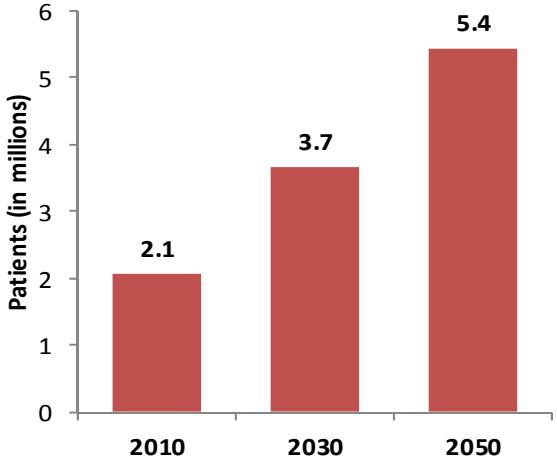
NIH estimates that the number of Americans with late stage AMD grew at a 1.7% CAGR from 1.8 million in 2000 to 2.1 million in 2010. That growth rate is expected to nearly double to 2.9% annually as 3.7 million Americans are expected to suffer from late stage AMD by 2030. This growth will primarily be driven by the aging of the population. By 2030, more than one in five Americans is expected to be age 65 or older according the US Census Bureau, up from 13% in 2010. Americans age 80 or older are expected to grow from 3.6% to 5.4% of the population over this time.

Exhibit 5 **US Population Age 65+ 2010 – 2050**



Source: US Census Bureau

Exhibit 6 **US Late Stage AMD Patients 2010 - 2050**



Source: National Eye Institute of NIH

How is AMD Treated?

During the early and intermediate stages of AMD, there are no medical treatment options. Patients can make nutrition and lifestyle choices, such as taking vitamins, exercising, and quitting smoking, to potentially slow the progression of the disease, but there are no drugs to treat any form of dry AMD. Once the disease progresses to wet AMD, the standard of care is drug treatment with an anti-VEGF therapy. These drugs are injected directly into the eye (intravitreal) and target a protein called vascular endothelial growth factor (VEGF) that stimulates new blood vessel growth. There are three commonly used anti-VEGF therapies:

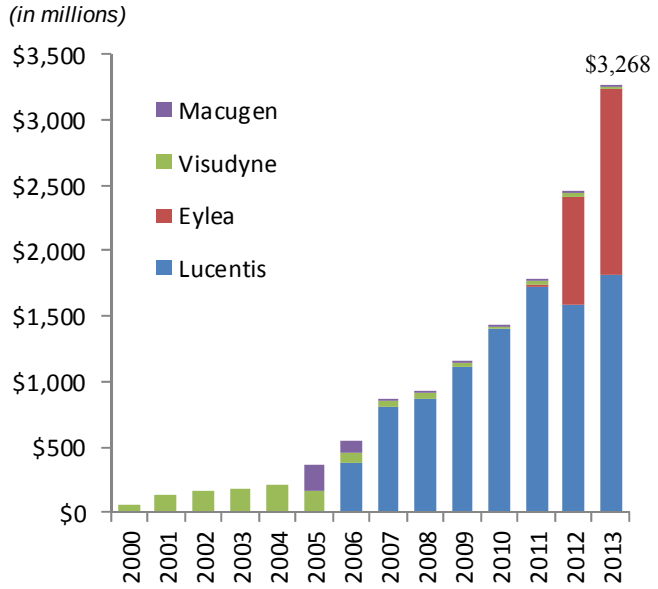
- Lucentis (ranibizumab) was approved in 2006 as a once-monthly injection for the treatment of wet AMD. The drug is sold by Genentech/Roche in the US and by Novartis in Europe and most other global markets.
- Eylea (aflibercept) was approved in 2011 as a bi-monthly injection (after three initial monthly injections) for wet AMD. The drug is sold by Regeneron in the US and by Bayer in Europe and most other global markets.
- Avastin (bevacizumab) is a drug from Genentech that is approved to treat several types of cancer. However, its chemical similarity to Lucentis has led to doctors using reformulated versions of the drug for wet AMD. This "off-label" use is due to Avastin being approximately 40 times cheaper than Lucentis therapy in the US.

While older options like Visudyne/photodynamic therapy (PDT) have been shown to slow the progression of wet AMD, anti-VEGF treatments are capable of reversing some of the damage and improving vision. These benefits have been shown to last for 2-3 years after initiation of therapy. However, more recent studies have indicated that visual acuity will once again diminish despite continued anti-VEGF treatment over a longer period of time.

How Big is the Wet AMD Market?

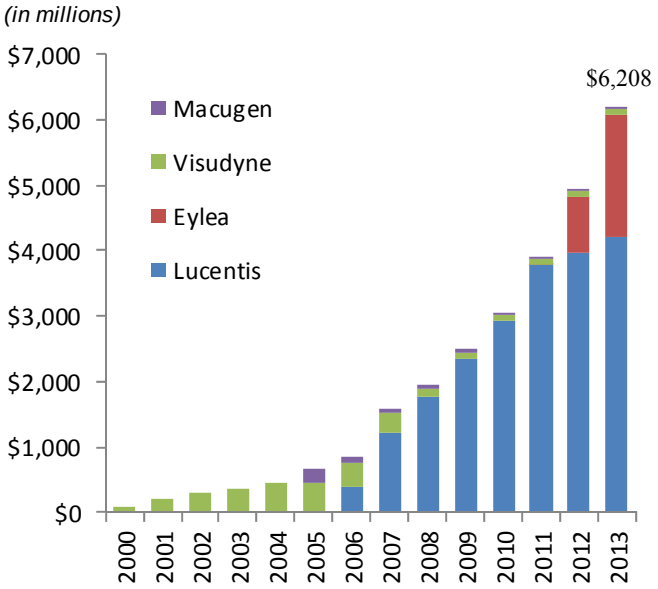
In 2013, sales of Lucentis and Eylea were over $3.2 billion in the US and nearly $6.1 billion worldwide. Older products, including Visudyne and Macugen, added another $100 million globally. These sales exclude off-label use of Avastin, which is estimated to account for approximately one-half of the US market and a one-quarter of the European market by volume. At branded pricing, this would equate to over $6 billion in the US and $10 billion globally for anti-VEGF treatments. While wet AMD is the primary use for these drugs, they are also used for other eye diseases, including retinal vein occlusion (RVO) and diabetic macular edema (DME). Over the past five years, the market for drugs approved to treat wet AMD has grown at a 26% CAGR driven primarily by Lucentis and Eylea.

Exhibit 7 **US Sales of Wet AMD Drugs: 2000 - 2013**



Source: Company filings and Gabelli & Company estimates

Exhibit 8 **Global Sales of Wet AMD Drugs: 2000 - 2013**



Source: Company filings and Gabelli & Company estimates

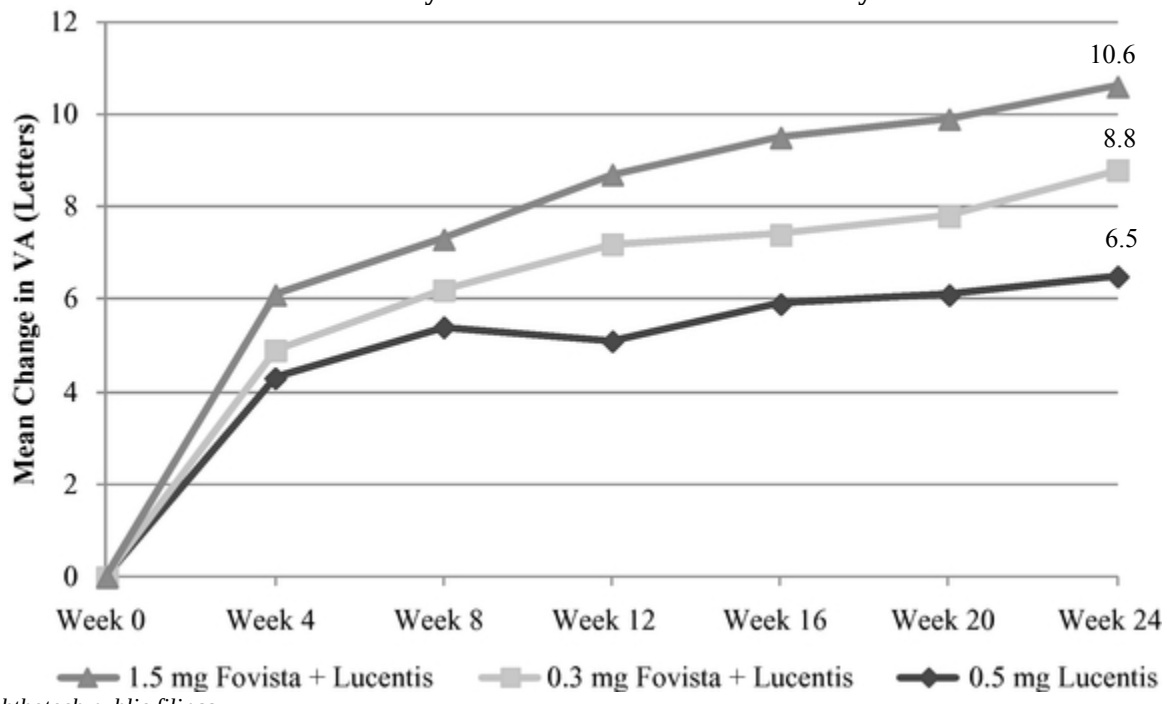
FOVISTA – THE NEXT GENERATION OF TREATMENT FOR WET AMD

Ophthotech's lead development product is Fovista, an anti-PDGF aptamer currently in Phase III development for treatment of wet AMD in combination with anti-VEGF therapy. Platelet derived growth factor (PDGF) plays a major role in blood vessel formation and development. By inhibiting PDGF, Ophthotech believes that Fovista removes protective cells (pericytes) from blood vessels, making them more susceptible to anti-VEGF therapy. Additionally, the company believes that Fovista could inhibit subretinal fibrosis caused by cells that are attracted by PDGF.

Phase II Results - Demonstrated Proof of Concept in Wet AMD

In June 2012, Ophthotech reported results from a 449-patient double-blinded Phase II trial comparing monthly Fovista + Lucentis (injected intravitrially, 30 minutes apart) to Lucentis monotherapy in patients with wet AMD. Two doses of Fovista (0.3mg and 1.5mg) were evaluated over 24 weeks with a primary endpoint of mean change in visual acuity (as measured by lines read on ETDRS standardized chart). At the 1.5mg high dose, Fovista + Lucentis resulted in an average 10.6 letter improvement vs. 6.5 letters for Lucentis monotherapy at 24 weeks, a statistically significant 62% benefit (p=0.019). There was a clear dose response between the 0.3mg and 1.5mg Fovista doses, and mean visual acuity improved at each time point for both Fovista arms. Secondary endpoints, including proportion of patients gaining fifteen or more letters, also favored Fovista combination therapy, though these did not meet statistical significance. Adverse events were similar among all three patient arms.

Exhibit 9 **Visual Acuity Results for Fovista Phase II Study**



Source: Ophthotech public filings

Phase III Program - Looking to Replicate Results

Ophthotech is currently enrolling patients in two Phase III trials comparing 1.5mg Fovista + Lucentis to Lucentis monotherapy that are similar in design to the successful Phase II study. The biggest differences are the study size (~622 patients each) and the duration of therapy (one year). The company only needs to replicate the Phase II results to reach its primary endpoint (visual acuity change) in Phase III. The increased enrollment size will more than double the number of patients in each trial compared to Phase II, providing an additional margin of safety through higher statistical power. Ophthotech also believes that the improved benefits over time for Fovista that were seen in Phase II could extend beyond 24 weeks, producing even better results at the one year endpoint.

The company has also initiated a third Phase III study to evaluate Fovista use with either Avastin or Eylea. This trial will also enroll approximately 622 patients and will have the same design and endpoints as the Lucentis-based trials. While we would expect the efficacy benefits to be similar among the different anti-VEGF therapies, we note that the injection volumes for both Avastin (1.25mg) and Eylea (2mg) are greater than that for Lucentis (0.5mg). Data from all three Phase III clinical trials are expected in the second-half of 2016, resulting in a filing with the FDA by the end of 2016.

Additional Fovista Studies

In addition to the three Phase III studies, Ophthotech plans to initiate several exploratory Phase II studies throughout 2014 and 2015. For wet AMD, these include combination studies looking at reducing the number of injections, treating patients who fail anti-VEGF therapy, and exploring the anti-fibrotic effects of Fovista. The company is also looking at Fovista monotherapy for other eye-related diseases that are impacted PDGF, such as Von Hippel-Lindau disease and proliferative vitreoretinopathy. Von Hippel-Lindau is a genetic disease estimated to occur in one out of every 36,000 patients (or approximately 8,000 people in the US) that causes the formation of tumors and cysts, including retinal angiomas. Proliferative vitreoretinopathy is a disease that occurs in 5-10% of patients with rhegmatogenous retinal detachment. Results from these Phase II exploratory studies would be expected beginning in the second half of 2015 and extending throughout 2016 and early 2017.

Novartis Partnership

In May 2014, Ophthotech licensed ex-US Fovista rights to Novartis in exchange for sales royalties and over $1 billion in upfront and potential milestones. Outside the US, Novartis is the market leader in wet AMD with Lucentis, which generated $2.4 billion of sales in 2013. Under the collaboration, Ophthotech is eligible to receive:

- Upfront payment of $200 million
- Potential Phase III enrollment milestones up to $130 million
- Potential ex-US marketing approval milestones up to $300 million
- Potential ex-US commercial milestones up to $400 million
- Royalties in the mid-30% range on ex-US sales of Fovista
- Similar royalties on the Fovista portion of sales from any potential co-formulated anti-VEGF/Fovista product
- Options on US rights for a co-formulated anti-VEGF/Fovista or Fovista pre-filled syringe product

In addition to securing significant funding and a leading commercial partner outside the US, this partnership also helps validate the science and data behind Fovista and PDGF.

Competition

With the positive Phase II results, Fovista is the only drug in development to demonstrate a statistically significant benefit over the current standard of therapy for wet AMD. We believe that Fovista is at least 2-3 years ahead of its nearest competitors in development and could ultimately be 4-5 years ahead of the closest anti-PDGF competitor. These potential competitors include:

- Squalamine (Ohr Pharma) is a twice-daily eye drop that targets VEGF, PDGF, and basic fibroblast growth factor (bFGF). Interim Phase II results of PRN (as needed) Lucentis +/- Squalamine in 62 patients showed a 65% improvement for Squalimine vs. placebo at 9 months, though this did not meet statistical significance (p=0.18). The interim data also showed no difference in the study's primary endpoint evaluating frequency of Lucentis use between Squalamine and placebo patients. Final Phase II data are expected in Q1 2015. While the interim data indicate a potentially competitive product to Fovista, we note that the ongoing Phase II trial's design and size are likely inadequate to determine the true profile of Squalamine. While Ohr anticipates moving directly into Phase III, we believe that a larger Phase II study with a controlled Lucentis dosing regimen may be necessary. Ohr must also find a way to finance any further studies since the clinical stage company ended March 2014 with less than $3.5 million of cash.

- REGN2176-3 (Regeneron/Bayer) is an intravitreal injection that combines Eylea with a novel antibody that directly targets PDGFR-β. This mechanism is slightly different from Fovista, which targets PDGF-BB and thus blocks interaction with the PDGF-β receptor. In February 2014, Regeneron initiated a Phase I trial of REGN2176-3 in wet AMD and could potentially move the product into Phase II by the first half of 2015.

- AGN-151200 (Allergan) is a dual *DARPin* product for intravitreal injection that targets VEGF and PDGF-B. This product is currently in preclinical development. Allergan recently reported Phase II results in wet AMD showing up to a 91% improvement in visual acuity for abicipar pegol, an anti-VEGF *DARPin* product, vs. Lucentis at 20 weeks. However, the study was small (64 patients across 3 arms) and did not demonstrate statistical significance. As an anti-VEGF drug, abicipar pegol could potentially be used in combination with Fovista. Allergan intends to move abicipar pegol into Phase III during the second quarter of 2015 but has not provided any update on AGN-151200. In addition to the manufacturing issues that are impacting the *DARPin* program, we would note that Valeant Pharmaceutical's high profile hostile takeover attempt for Allergan could create further delays.

- ISONEP (Lpath/Pfizer) is an antibody that targets sphingosine-1-phosphate (S1P) and has been formulated for intravitreal injection. The drug is currently being evaluated in Phase II for both monotherapy and combination therapy with anti-VEGF for wet AMD. Pfizer currently has the rights to the drug but is seeking to divest those rights following delays for the Phase II program. Data from the ongoing study are expected later this year.

Exhibit 10 **Pipeline of New Drug Classes in Development for Wet AMD**

Drug	Company	Targets	Dosing	Clinical Stage
Fovista	Ophthotech/Novartis	PDGF-BB	Monthly intravitreal	Phase III
Squalamine	Ohr Pharmaceuticals	VEGF/PDGF/bFGF	2x day eye drop	Phase II
iSONEP	Lpath/Pfizer	S1P	Monthly intravitreal	Phase II
REGN2176-3	Regeneron/Bayer	VEGF/PDGFR-β	Intravitreal	Phase I
DE-120	Santen	VEGF/PDGF	"	" I
X-82	Xcovery Vision	VEGF/PDGFR	Oral	" I
AGN-151200	Allergan	VEGF/PDGF-B	Intravitreal	Preclinical
NT-506	Neurotech	PDGF	Implant	"

Source: Company filings, www.clinicaltrials.gov, and Gabelli & Company estimates

Market Opportunity for Fovista

The market for wet AMD is expected to remain dominated by the anti-VEGF therapies Lucentis, Eylea, and Avastin over the next several years. By 2018, the global market for Lucentis and Eylea could surpass $9 billion even with the continued off-label use of Avastin. We expect the introduction of add-on anti-PDGF therapies, starting with Fovista, to be the next inflection point for wet AMD therapies and could potentially double the market. While Eylea and Lucentis are hurt by off-label Avastin, there currently does not appear to be any comparable off-label PDGF product to cannibalize market share. Since anti-PDGF therapies are expected to work with any anti-VEGF drug, the anti-PDGF market could eventually become bigger than anti-VEGF therapies for wet AMD.

Ophthotech expects to report Phase III results and file for approval of Fovista in 2016. This could lead to approval in mid-to-late 2017. Based on this timeline and a price point equivalent to that of current anti-VEGF drugs (~$2,000 per injection), we believe that Fovista net sales could reach $1.2 billion in the US and $1.8 billion worldwide by 2020. Given the current stages of development for competing therapies, we expect Fovista to be the only anti-PDGF drug on the market through at least 2020. Even with additional competition beyond 2020, we believe that Fovista could eventually surpass $4 billion in peak sales.

ZIMURA – TARGETING THE DRY AMD MARKET

Ophthotech's second product in development is Zimura, an aptamer that inhibits complement factor C5 and is expected to begin Phase 2/3 studies for geographic atrophy (GA) later this year. GA is an advanced form of dry AMD that accounts for up to one-third of late AMD cases and effects an estimated 8 million people globally. Studies have indicated that inflammatory responses, including those caused by the complement system, play a role in the progression of dry AMD. The company believes that targeting the C5 compliment pathway could reduce the progression of tissue damage associated with GA and dry AMD. There are currently no approved treatments for dry AMD or GA.

Clinical Evidence for Benefits of Complement Inhibition in GA

The complement system consists that of several proteins and pathways that make up part of the body's immune system. Complement pathways have been implicated in several diseases, and validated complement targets for drug treatment include C1 for hereditary angioedema (Cinryze and Berinert) and C5 for paroxysmal nocturnal hemoglobinuria (Soliris). In August 2013, Roche announced positive Phase II results for its complement factor D inhibitor, lampalizumab. This study provided the first clinical evidence that inhibition of complement factors could slow the progression of GA. Patients given monthly intravitreal injections of lampalizumab had a 20.4% reduction in the rate of GA progression at 18 months vs. placebo patients ($p<0.1170$ but considered statistically significant under pre-specified criteria). Among the 57% of patients who were positive for a compliment factor 1 biomarker, there was a 44% reduction in the rate of GA progression ($p<0.005$) for monthly lampalizumab vs. placebo.

Ophthotech has completed a Phase 1/2a study to evaluate Zimura in patients with GA. The 47-patient study was split between two intravitreal injection doses (0.3mg and 1mg) given at weeks 0, 4, 8, 24, and 36. While GA lesions continued to grow from baseline, there was a dose-dependent response at week 24 with average growth of $0.78mm^2$ for 1mg dose vs. $1.00mm^2$ for the 0.3mg dose. By 48 weeks, there was little difference between the two arms ($+1.71mm^2$ vs. $+1.73mm^2$ for high and low doses, respectively).

While the Phase 1/2a data for Zimura indicate a potential efficacy signal, the drug has not yet demonstrated proof of concept for the role of C5 in dry AMD. Using data from this study and the lampalizumab study, Ophthotech plans to initiate a Phase 2/3 study of Zimura later this year. Interim results from this study could be available by the end of 2016.

Competition

There are several competing drugs in development for GA/dry AMD that target the complement system or other pathways. Lampalizumab is the most advanced of these competitors with proof-of-concept Phase II data. Roche is currently enrolling an open-label Phase II extension study for the drug but has not given an indication of when the drug will enter Phase III. Other potential competitors to Zimura include:

- LFG316 (Novartis/MorphoSys) is a monthly intravitreal injection that also targets complement factor C5. An 18-month Phase II study for treatment of GA is currently enrolling patients. The drug is also in Phase II for multifocal choroiditis and panuveitis.

- AL-78898A (Novartis) is a monthly intravitreal injection targeting complement factor C3. A Phase II study for GA had been initiated in 2012 but was terminated later that year.

- Other drugs in active Phase II studies for GA with mechanisms outside the complement system include corticosteroids (Iluvien from Alimera), neuroprotectants (brimonidine from Allergan), visual cycle modulators (emixustat from Acucela), vasodilators (MC-1101 from MacuCLEAR), and amyloid-β antagonists (GSK933776 from GlaxoSmithKline).

Exhibit 11 Pipeline of Potential New Drug Classes for Geographic Atrophy/Dry AMD

Drug	Company	Mechanism of Action	Formulation	Clinical Stage
Emixustat	Acucela/Otsuka	Visual cycle modulator	Once-daily oral	Phase II/III
MC-1101	MacuCLEAR	Vasodilation	2x day eye drop	Phase II/III
Lampalizumab	Roche	Complement Factor D inh.	Monthly intravitreal	Phase II
Brimonidine	Allergan	α2-adrenergic agonist	Implant	Phase II
Iluvien	Alimera	Corticosteroid	"	Phase II
Zimura	Ophthotech	C5 inhibitor	Monthly intravitreal	Phase II
GSK933776	GlaxoSmithKline	Amyloid β inh.	Intravenous infusion	Phase II
LFG316	Novartis/MorphoSys	C5 inhibitor	Monthly intravitreal	Phase II
AL-78898A	Alcon (Novartis)	C3 "	" "	Phase II
RN6G	Pfizer	Amyloid β inh.	Intravenous infusion	Phase II
MA09-hRPE	Advanced Cell Tech.	RPE stem cells	Transplant	Phase I/II
HuCNS-SC	StemCells	CNS stem cells	"	Phase I/II
Adipocell	Bioheart	Adipose stem cells	"	Phase I
CLG561	Alcon (Novartis)		Intravitreal	Phase I

Source: Company filings, www.clinicaltrials.gov, and Gabelli & Company estimates

Market Opportunity for Zimura

Currently, there are no approved drug treatments for geographic atrophy or dry AMD. However, the potential size of the market for dry AMD with effective therapies has been estimated as high as $30 billion worldwide. A market approaching this size would likely require treatments that are capable of either stopping or reversing the progression of geographic atrophy. Based on clinical trial results from Zimura, lampalizumab, and other products that have completed Phase II studies, the first generation of drugs for GA and dry AMD are likely to have modest effects on slowing the progression of the disease without actually stopping or reversing it.

We would expect the market for first-generation dry AMD drugs to look similar to the initial market for wet AMD drugs prior to the launch of Lucentis. The first two drugs for wet AMD, Visudyne and Macugen, were only able to slow the progression of the disease. These drugs reached combined sales of approximately $350 million in the US and $650 million globally before the introduction of Lucentis, a drug that drastically reversed the damage of the disease and immediately took over 90% of the market.

We estimate that Zimura could reach peak sales of $300-500 million. While the drug could reach the market as early as 2018 depending on the Phase 2/3 data, we would expect an additional pivotal study to push the approval timeline beyond 2020. Given the uncertainty around the development timeline and the limited existing clinical data for both Zimura and the C5 pathway for treatment of GA/dry AMD, our estimates and valuation exclude any revenue contribution from Zimura.

OPHTHOTECH MANAGEMENT – PIONEERS IN WET AMD

Ophthotech's management team is led by the company's two co-founders – Chairman/CEO David Guyer and Vice Chairman/President Samir Patel. Both Drs. Guyer and Patel are pioneers in the development of treatments for wet AMD. Prior to starting Ophthotech, they founded another ophthalmology company focused on aptamer drugs called Eyetech. At Eyetech, they successfully developed and launched Macugen, the first aptamer and the first anti-VEGF drug for wet AMD to be approved by the FDA. In November 2005, they sold Eyetech for $935 million to OSI Pharmaceuticals just as Phase III data were being reported for the competing anti-VEGF product, Lucentis.

We view Macugen as both a success story and cautionary tale. The Eyetech team was able to develop a drug with a novel mechanism of action for wet AMD. The drug also reached $185 million in US sales and became the market leader in 2005, its first year on the market. However, sales rapidly declined with the approval of Lucentis in 2006, and OSI elected to exit the eye care market shortly thereafter. This decision by OSI created a second opportunity for Drs. Guyer and Patel. After founding Ophthotech in 2007, they acquired the rights to particular anti-PDGF aptamers from OSI for payment of $4 million upfront, 3 million shares of preferred stock, and future milestone and royalty payments. Drs. Guyer and Patel had been developing these pre-clinical anti-PDGF aptamers, which included Fovista, at Eyetech prior to the sale of the company to OSI.

We believe that Ophthotech's management team is capable of once again bringing a first-in-class aptamer drug to market with Fovista. We also expect Fovista to have a greater commercial opportunity than Macugen for several reasons:

- *Wider range of activity*. Macugen was designed to specifically target VEGF isoform 165 and avoid isoform 121. This selective targeting proved to be less efficacious than that of pan-VEGF inhibitors like Lucentis, Avastin, and Eylea. Fovista targets PDGF-BB, and *in vitro* studies have shown that the drug halts binding of both PDGF-AB and PDGF-BB to their receptors, PDGFR-α and PDGFR-β. We believe that this range of targeting is comparable to, if not wider than, that of the drug's closest competitors.

- *Proof of concept vs. SOC.* We believe that the clinical profile of Fovista is much better established going into Phase III as compared to Macugen. The Phase II study for Fovista demonstrated a statistically significant improvement for combination therapy vs. the current standard of care (SOC), Lucentis monotherapy. This efficacy raises the standard for future competitors, and the data helped establish a single-dose Phase III trial design. Conversely, the pivotal studies for Macugen were multi-dose Phase II/III studies vs. placebo. Prior to those results, Eyetech had only conducted small safety studies for the drug.

- *Greater lead time on competitors.* Macugen had less than an 18 month lead over Lucentis in coming to market. We believe that Fovista currently has at least a 2-3 year lead over competing PDGF inhibitors. We expect Fovista to be approved by the end of 2017 and would not expect a competing anti-PDGF drug to reach the wet AMD market before 2020.

- *No off-label competition*. Macugen was forced to compete with both high-cost Lucentis and low-cost off-label Avastin. Lucentis is a fragmented version of the Avastin monoclonal antibody, and doctors were able to use the cancer drug Avastin off-label even before Lucentis was approved. We would not expect to see a similar situation for Fovista or other anti-PDGF drugs.

- *Larger market for wet AMD*. In 2013, the global market for drugs approved to treat wet AMD was $6.2 billion. This compares to a $450 million worldwide market in 2004 when Macugen was first approved. By 2018, the global market could surpass $9 billion, or 20x the size of the market when Macugen was introduced. This large market opportunity would allow Fovista to be a profitable product even with significant competition from other next-generation wet AMD therapies.

ESTIMATES AND VALUATION

Over the next three years, Ophthotech's primary focus will be the Phase III development program for Fovista in wet AMD and the Phase II/III study for Zimura in GA/dry AMD. We estimate that this will require over $400 million of R&D spending from 2014-2017 prior to the expected launch of Fovista in 2018. The company has been able to finance itself to date through several vehicles, including:

- $175.6 million from IPO of 8.74 million shares in September 2013 at $22 per share
- $83.3 million from Novo A/S through two financing tranches (May 2013 and January 2014) in exchange for future royalties, with the potential for a third tranche of $41.7 million
- $55.4 million from a February 2014 secondary offering of 1.9 million shares at a price of $31.50 per share
- $200 million upfront payment from Novartis in exchange for ex-US rights to Fovista, with the potential for an additional $130 million of enrollment milestones and $700 million of approval/commercial milestones

Ophthotech ended the first quarter with $263 million of cash and no debt. We believe that this cash, along with the upfront and potential milestones from Novartis, will be enough to finance the company until profitability in 2018 without the need for the third tranche of $41.7 million from Novo A/S or any other additional source of capital.

We expect Fovista to be approved in late 2017 and launched in early 2018. By 2020, we estimate that global sales of Fovista could reach $1.8 billion, resulting in revenues of nearly $1.4 billion for Ophthotech from US sales and international royalties. We would expect the product to be highly profitable given the high price point for wet AMD therapy and the relatively small sales force required to market these products. Ophthotech believes that it could market Fovista to the 2,000 retinal specialists in the US with a 100-person specialty sales force. We expect operating margins to surpass 50% in 2020, resulting in earnings of more than $12 per share.

Table 1

Ophthotech Corp.
Income Statement
2013A – 2020P

($ in millions except per share data)

FYE 12/31	**2013A**	**2014E**	**2015P**	**2016P**	**2017P**	**2018P**	**2019P**	**2020P**
Product Sales	$ -	$ -	$ -	$ -	$ -	$ 450	$ 850	$ 1,200
Royalties	-	-	-	-	-	24	96	192
Milestones	-	250	80	-	75	75	-	-
Total Revenue	**$ -**	**$ 250**	**$ 80**	**$ -**	**$ 75**	**$ 549**	**$ 946**	**$ 1,392**
COGS	-	-	-	-	-	96	211	312
SG&A	14	28	32	35	65	175	215	260
R&D	33	78	140	115	85	95	120	145
Operating Income	$ (47)	$ 144	$ (92)	$ (150)	$ (75)	$ 183	$ 400	$ 675
Interest/Other	10	(1)	(1)	(1)	(0)	(1)	(2)	(4)
Taxes	-	29	-	-	-	38	136	204
Net Income	$ (57)	$ 116	$ (91)	$ (149)	$ (75)	$ 152	$ 290	$ 523
Diluted Shares O/S	9	33	34	35	37	40	42	43
Diluted EPS	**($6.34)**	**$3.60**	**($2.70)**	**($4.25)**	**($2.05)**	**$3.80**	**$7.00**	**$12.15**
Cashflow/(burn)	$ (54)	$ 122	$ (84)	$ (141)	$ (68)	$ 162	$ 300	$ 535

Source: Company filings and Gabelli & Company estimates

Our valuation for OPHT is based on a 14x multiple of EBITDA starting in 2019, the second full year of Fovista sales. Prior to this, we use a 15% annual discount rate on the 2019 valuation and apply a second discount based on the expected stage of development for Fovista. We use a 25% discount from 2014-2016 to reflect Phase III development risk and a 15% discount in 2017 to reflect new drug application (NDA) approval risk. Using this method, we arrive at a PMV of $80 per share for 2015, growing to $316 per share in 2020.

We are initiating coverage on OPHT with a Buy recommendation and believe that the company offers one of the most attractive investment opportunities in the developmental biotech market. Ophthotech is one of the few clinical stage biotech companies with an asset that:

- Addresses a large and fast growing market ($6.2B for wet AMD drugs, growing at 26% annually)
- Demonstrated statistically significant clinical superiority to the standard of care (62% improvement for Fovista + Lucentis vs. Lucentis monotherapy, p =0.019)
- Has a 2-3 year lead time on competitors
- Is being developed by an experienced management team (co-founders David Guyer and Samir Patel, who developed Macugen, the first anti-VEGF drug for wet AMD)
- Can be financed with existing cash on hand ($263 million at end of Q1 plus $200 million from Novartis)

We would also note that Ophthotech's market cap of $1.4B is less than 1/20th the size of that for Regeneron, the manufacturer of Eylea. While Regeneron has other products approved and in late stage development, Eylea is the company's largest product and is estimated to account for $15-$20 billion of the company's $30 billion market cap. On June 13, 2012 when the Phase II results for Fovista were reported, Regeneron shares fell by nearly $16 per share. This equated to a $1.5 billion decline in market cap, more the entire market cap of Ophthotech. Additionally, Valeant's current proposal to acquire Allergan includes a contingent value right (CVR) associated with Allergan's *DARPin* program for wet AMD. Valeant is offering a CVR valued up to $25 per share, or approximately $7.7 billion, based on future *DARPin* net sales.

We believe that Ophthotech's shares are significantly undervalued based on both the opportunity for Fovista and the valuation of the company's closest competitors. While we caution that investors will have to wait until 2016 for the pivotal Phase III data, we note that results from exploratory Phase II studies could serve as interim catalysts in 2015. Ophthotech shares currently trade at a 50% discount to our 2015 Private Market Value of $80 per share.

Table 2

Ophthotech Corp.
Private Market Value Analysis
2014E – 2020P

($ in millions except per share data)

FYE 12/31	**2014E**	**2015P**	**2016P**	**2017P**	**2018P**	**2019P**	**2020P**
Revenue	$ 250	$ 80	$ -	$ 75	$ 549	$ 946	$ 1,392
EBITDA	144	(92)	(150)	(75)	190	425	725
Valuation Multiple	- x	- x	- x	- x	- x	14 x	14 x
Annual Discount Rate	15%	15%	15%	15%	15%	0%	0%
Total Private Market Value	$ 2,959	$ 3,402	$ 3,913	$ 4,500	$ 5,175	$ 5,951	$10,151
Clinical Stage Discount Rate	25%	25%	25%	15%	0%	0%	0%
Risk-Adjusted Total PMV	$ 2,219	$ 2,552	$ 2,935	$ 3,825	$ 5,175	$ 5,951	$10,151
Plus: Net Cash	333	248	107	40	202	501	1,036
Less: Option Payments (a)	(128)	(143)	(159)	(210)	(305)	(373)	(671)
Equity Private Market Value	$ 2,424	$ 2,657	$ 2,883	$ 3,654	$ 5,071	$ 6,079	$10,516
Shares Outstanding	33	33	33	33	33	33	33
PMV per Share	**$73**	**$80**	**$87**	**$110**	**$152**	**$182**	**$316**
Current Market - Discount to PMV	*45%*	*50%*	*54%*	*64%*	*74%*	*78%*	*87%*

(a) After-tax payments to buy out warrants at PMV

Source: Company filings and Gabelli & Company estimates

Other Companies Mentioned:

Acucela Inc.	(AUCL - OTC)	Novartis AG	(NVS – NYSE)
Advanced Cell Technologies	(ACTC - ")	Ohr Pharmaceutical, Inc.	(OHRP – NASDAQ)
Alimera Sciences	(ALIM - NASDAQ)	Otsuka Corp.	(4768 – Tokyo)
Allergan Inc.	(AGN - NYSE)	Pfizer Inc.	(PFE – NYSE)
Bayer AG	(BAYN – XETRA)	Regeneron Pharmaceuticals	(REGN - NASDAQ)
Bioheart Inc.	(BHRT – OTC)	Roche Holding AG	(ROG – SIX)
GlaxoSmithKline plc	(GSK – NYSE)	Santen Pharmaceutical Co.	(4536 – Tokyo)
Lpath Inc.	(LPTN – NASDAQ)	StemCells Inc.	(STEM – NASDAQ)
MorphoSys AG	(MOR – XETRA)	Valeant Pharmaceutical	(VRX – NYSE)

I***, Kevin Kedra,*** the Research Analyst who prepared this report, hereby certify that the views expressed in this report accurately reflect the analyst's personal views about the subject companies and their securities. The Research Analyst has not been, is not and will not be receiving direct or indirect compensation for expressing the specific recommendation or view in this report.

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Important Disclosures

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Ratings

Analysts' ratings are largely (but not always) determined by our "private market value," or PMV methodology. Our basic goal is to understand in absolute terms what a rational, strategic buyer would pay for an asset in an open, arms-length transaction. At the same time, analysts also look for underlying catalysts that could encourage those private market values to surface.

A **Buy** rated stock is one that in our view is trading at a meaningful discount to our estimated PMV. We could expect a more modest private market value to increase at an accelerated pace, the discount of the public stock price to PMV to narrow through the emergence of a catalyst, or some combination of the two to occur.

A **Hold** is a stock that may be trading at or near our estimated private market value. We may not anticipate a large increase in the PMV, or see some other factors at work.

A **Sell** is a stock that may be trading at or above our estimated PMV. There may be little upside to the value, or limited opportunity to realize the value. Economic or sector risk could also be increasing.

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