

LUCY LU, M.D., Vice President lucy.lu@fac.com tel: 212. 273.7126 fax: 212.273.7198

Company Headquarters: New York, NY Company Website: www.eyetech.com

Rating Current Price Price Target 52 Wk Price Range 30-Day Avg Daily Vol Market Capitalization Shares Outstanding Cash Cash/Share Debt/Capital Book Value Bask Value	Neutral \$27.57 NA \$49.12 - \$25.55 1.2 M \$1,186 M 43 M \$211.5 M \$4.92 0% \$131.3 M \$2.16
	- / -
Book Value/Share	\$3.16
Dividend Yield 3 Yr EPS Growth	NA NA
FY End	December

Earnings Per Share									
	2004A 2005E 2006E								
Q1	\$(0.44)	\$(0.28)	NA						
Q2	\$(0.77)	\$(0.16)	NA						
Q3	\$(0.60)	\$(0.09)	NA						
Q4	\$(0.72)	\$(0.05)	NA						
Year	\$(2.56)	\$(0.57)	\$1.23						
P/E	NM	NM	22x						

Note: Numbers may not add because of rounding. NA: Not Available.

Revenue (\$mil)									
	2004A 2005E 2006E								
Q1	\$11.7	\$34.3	NA						
Q2	\$12.6	\$47.0	NA						
Q3	\$13.5	\$55.9	NA						
Q4	\$11.6	\$64.9	NA						
Year	\$49.4	\$202.1	\$483.2						
RM	24.0x	5.9x	2.5x						



Source: Bigcharts.com

# EQUITY RESEARCH

### **COMPANY REPORT**

## **INITIATING COVERAGE**

HEALTHCARE Biotechnology

# NEUTRAL

## Eyetech Pharmaceuticals, Inc. EYET - \$27.57

March 31, 2005

## Initiating Coverage with a Neutral Rating

- We are initiating coverage of Eyetech Pharmaceuticals with a Neutral rating. Eyetech's Macugen is the first FDA-approved therapy for the treatment of all types of wet AMD. Eyetech, along with partner Pfizer, launched Macugen in the United States in January 2005.
- While it has a two-year lead over a competing drug, Genentech's Lucentis, there is wide perception among some physicians that Lucentis is a superior drug. Therefore, we believe that Eyetech has limited upside potential until investors can better gauge how the competitive landscape for AMD will evolve.
- We will have results from the first of Lucentis' Phase III studies, MARINA, around mid-2005. If Lucentis' data demonstrates clear superiority over Macugen, we believe Eyetech's downside risk is as many as 10 points. However, if Lucentis is only comparable to Macugen, we believe Eyetech may gain approximately 10 points on the news.
- We believe the most likely scenario is somewhere between these two extremes and that is currently reflected in Eyetech's valuation. We have modeled our U.S. Macugen sales accordingly: \$152 million for 2005, \$406 million for 2006, \$403 million for 2007, and \$388 million for 2008.
- In summary, we advise investors to stay on the sideline at this time; upon reviewing data from MARINA, we can better assess the investment opportunities in AMD and will revisit our investment stance on Eyetech.

Specific required disclosures with regard to the companies mentioned in this publication can be found beginning on page 14. Reg A/C certification can be found on page 14.

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### INVESTMENT OVERVIEW

We are initiating coverage of Eyetech Pharmaceuticals with a Neutral rating. Eyetech's lead drug, Macugen (pegaptanib), is the first anti-angiogenesis therapy for the treatment of the wet form of age-related macular degeneration (AMD), the leading cause of loss of vision in the elderly, with an incidence of 200,000 cases in the United States. Macugen is partnered with Pfizer and was launched in the United States in January 2005. The two companies will share profits on a 50/50 basis in the United States. Outside the United States, Pfizer will commercialize Macugen and pay Eyetech a royalty on sales.

Over the next two years, Macugen's primary competition will be photodynamic therapy (PDT) with Visudyne (verteporfin, QLT Inc.), which is an intravenous administration of a photosensitizer, followed by a laser treatment. In our view, these two therapies are comparable in efficacy. Macugen's main advantage is its broad label that covers all subtypes of AMD. Both therapies slow down disease progression, and maintain but do not improve visual acuity (VA) in the majority of patients. Therefore, although we view Macugen as a breakthrough therapy that addresses a large market, we believe that there are still significant unmet needs in the AMD market. The dynamics of this market are also changing rapidly—several new therapies are in advanced-stage testing and will generate data that could have a direct impact on Macugen 's commercial potential. Starting in 2007, the most important competition for Macugen will, we believe, be Lucentis (ranibizumab, Genentech). There is wide perception among some retinal specialists that Lucentis is a superior drug, and we have heard a great deal of anecdotal evidence from them that Lucentis is more rapid-acting and actually improves versus just stabilizing vision in many patients.

Therefore, we believe that Eyetech has very limited upside potential in the near term until investors can better gauge how the competitive landscape for AMD will evolve. Lucentis is currently in pivotal Phase III trials, and we will have results from the first of Lucentis' studies, MARINA, around mid-2005. We believe both clinicians and investors will make preliminary comparisons of the two therapies. Although MARINA only enrolled patients with two out of three subtypes of wet AMD and is not exactly comparable to Macugen's pivotal VISION program, we believe how it compares to data from Macugen's VISION data will have a substantial impact on Eyetech's share price.

### Valuation

If Lucentis' data from MARINA demonstrates clear superiority over Macugen, i.e., 20% of the patients gain three or more lines in VA after one year of therapy, versus 6% in Macugen's VISION trial, we believe that Lucentis will dominate the market starting in 2007 and would likely revise our 2008 Macugen U.S sales estimate to \$295 million, as a result. The downside risk is as many as 10 points (Eyetech to trade to around \$18) in this scenario. On the other hand, if Lucentis is only comparable to Macugen (i.e., 10% three-line gainers), we believe that Eyetech may gain as many as 10 points on the news and that, because Macugen has a first-mover advantage, it will continue to dominate the market after 2007. We would likely revise our 2008 Macugen U.S. sales estimate to \$491 million. Based on the record of past physician anecdotal evidence, we believe the most likely scenario is somewhere between these two extremes, which we believe is currently reflected in Eyetech's stock price, and we have modeled our Macugen sales accordingly. Our U.S. Macugen sales estimates are \$152 million for 2005, \$406 million for 2006, \$403 million for 2007, and \$388 million for 2008, with projected profitability in 2006.

In summary, we believe that Eyetech is unlikely to have any significant price movement until we see the data from Lucentis' MARINA trial, at which point we can make a better assessment of the investment opportunities in AMD. We advise investors to stay on the sideline at this time; upon reviewing data from MARINA, we will revisit our investment stance on Eyetech.

### **COMPANY OVERVIEW**

### **Company Background**

Eyetech Pharmaceuticals, Inc. is a biopharmaceutical company that specializes in the development and commercialization of novel therapeutics to treat diseases of the eye, with a focus on diseases affecting the retina. The company has a collaboration agreement with Pfizer Inc. to co-promote Macugen for the treatment of the wet form of age-related macular degeneration.

### Age-Related Macular Degeneration

The retina is the lining in the back of the eye that enables vision. The central portion of the retina is called the macula and it is responsible for acute central vision and high-resolution visual acuity necessary for color recognition, reading, and driving. The center of the macula is called the fovea, containing the foveal avascular zone, which does not have blood vessels in healthy eyes. AMD is a deterioration of the macula, leading to irreversible loss of the ability to read, recognize faces, and drive. It is a chronic and progressive condition, characterized by a central blind spot, distortion of objects, or blurred vision. There are two types of AMD: the atrophic (dry) type and the neovascular, exudative (wet) type. Dry AMD is characterized by deposits of yellowish debris under the retina called drusen. Patients with early stage dry AMD experience minimal visual impairment. Dry AMD can progress to the late stages with large areas of atrophy in the retina called geographic atrophy. When geographic atrophy affects the fovea, significant vision loss can occur from the central blind spot (scotoma). There is no treatment for dry AMD at present, although some studies suggest that multivitamins with antioxidants and lutein may be of benefit. Approximately 10%-20% of patients with dry AMD will progress to the more aggressive and severe wet AMD. Wet AMD usually causes rapid vision loss due to the growth of abnormal blood vessels under the retina called choroidal neovascularization (CNV). The abnormal blood vessels bleed and leak fluid which result in fibrovascular scarring in the retina that destroys the photoreceptor cells and cause subsequent vision loss. Over 90% of patients diagnosed with wet AMD have subfoveal CNV, which means the lesions or abnormal newly developed blood vessels are located directly under the fovea.

Wet AMD accounts for 10% of cases but is responsible for 90% of the severe vision loss associated with AMD. It affects 1.6 million people in the United States and has an incidence of 200,000 cases per year. It is the leading cause of severe, irreversible blindness in the elderly in developed countries, often within months after the diagnosis is made. The most amount of vision deterioration typically takes place within the first six months of diagnosis. Many patients with AMD in one eye will eventually also develop the disease in the other eye. We expect the incidence of wet AMD to increase over the coming years as the U.S. population ages.

Wet AMD is classified by the appearance of leakage of fluorescein, a yellow dye that glows in visible light, from new blood vessels seen on fluorescein angiography, as summarized in Exhibit 1. Predominantly classic lesions are the most aggressive and lead to more rapid vision loss than other subtypes. Occult lesions tend to have the least rapid rate of vision loss.

#### EXHIBIT 1: Neovascular AMD Classification by Angiography Sources: Medscape.com, Company Report, and First Albany Capital

and First Albany	Capital	
Туре	Description	% of wet AMD
Classic	Early phase of angiogram: bright areas of fluorescein leakage with well-demarcated margins in the retina	< 10/
	Late phase of angiogram: margins of hyperfluorescent areas become blurred due to progressive leakage of fluorescein	< 1%
Occult	Two possible patterns:	
	<ol> <li>Bright, speckled areas of fluorescein leakage seen in the late phases of the angiogram – source of leakage cannot be determined from the early phases</li> </ol>	40%
	(2) Bright areas of stippled hyperfluorescence due to detachment of retinal pigment epithelium (a layer of cells in the retina) in the early-mid phases of the angiogram	
Predominantly Classic	Classic and occult components with classic CNV occupying 50% or more of the area of the entire lesion	25%
Minimally Classic	Classic and occult components with classic CNV occupying less than 50% of the area of the entire lesion	35%

### Macugen for AMD

The pathogenesis of wet AMD has not been completely elucidated, but growth factors and cytokines such as vascular endothelial growth factor (VEGF) are believed to play a significant role in stimulating the development of CNV. Multiple studies have shown VEGF is the common denominator in wet AMD and is over-expressed in CNV. Increased levels of VEGF are linked to neovascularization (new blood vessel formation) and increased permeability (leakage) of these newly formed vessels. Macugen is a PEGylated (combined with polyethylene glycol) aptamer [a strand of oligonucleotide (similar to DNA or RNA)] that specifically inhibits the 165-amino-acid isoform of VEGF (VEGF165) by preventing it from binding to its receptor. Although there are different VEGF isoforms, VEGF165 is believed to play an important role in the abnormal blood vessel growth and leakage associated with wet AMD. The specificity of Macugen for VEGF165 could theoretically allow maximal efficacy with minimal adverse effects and because Macugen is an aptamer, it is also less likely to cause an immunologic response than other biologic agents, such as antibodies.

Macugen was approved to treat all types and lesion sizes of wet AMD by the FDA in December 2004, and is the first in a new class of ophthalmic drugs that targets angiogenesis as the underlying cause. Macugen 0.3 mg (the approved dose) is delivered locally into the back of the eye via an intravitreal injection once every six weeks.

The approval is based on Macugen's pivotal VISION program (Exhibit 2), which consisted of two randomized, double-masked, sham-controlled, and dose-ranging trials that compared 0.3 mg, 1.0 mg, and 3.0 mg intravitreal injections of Macugen versus sham injection into one eye per patient once every six weeks. The study enrolled patients with all three subtypes of wet AMD and allowed them to receive PDT with Visudyne at physician's discretion, although 75% of the patients never received PDT. The primary endpoint, based on a pooled analysis of the two trials involving a total of 1,186 patients, was the percentage of patients losing fewer than 15 letters

(three lines) of VA measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. At 54 weeks, 70% of patients on Macugen 0.3 mg had lost fewer than three lines of vision, compared to 55% of those receiving sham injections. Macugen also reduced the rate of VA deterioration—at the end of the 54 weeks, patients in the sham group experienced a mean loss in VA of approximately 15 letters, versus approximately eight letters in the Macugen 0.3mg arm. Two other measures that retinal specialists look to are the percentages of patients who 1) gained three or more lines, and 2) gained zero or more lines. Macugen improved both measures at 54 weeks in VISION: 1) 6% of patients receiving Macugen 0.3mg gained three or more lines versus 2% in the sham group, and 2) 33% versus 23%. Macugen's therapeutic benefit was evident in all subtypes of AMD. Overall, the drug had a favorable safety profile without causing any systemic adverse events. In the study, the most noticeable serious adverse events were injection-related endophthalmitis (a potentially serious inflammation of the eye) with an incidence of 0.16% per injection, or 1.3% per patient, per year, during the first year of the VISION trials, which decreased during the second year of the VISION trials with standardizing sterilization techniques. The injections were otherwise well tolerated without causing increased intraocular pressure (IOP), which is sometimes seen with other intravitreal injections.

### EXHIBIT

2: Macugen's VISION Trials Source: New England Journal of Medicine and First Albany Capital

Macugen (pegaptanib)
VISION (VEGF Inhibition Study in Ocular Neovascularization)
Phase III, randomized, sham-controlled, double masked, international (US, Canada, Europe Israel, Australia, S. America) studies involving 1186 patients who were randomized to one of the four arms: sham, 0.3 mg, 1 mg, 3 mg every 6 weeks for 48 weeks (9 treatments total); PDT allowed per physician discretion
Average age: 75 Mean Baseline VA: 53 letters All subtypes of wet AMD allowed
% of patients losing <15 letters (3 lines) of VA at week 54
Macugen: 70% Placebo: 55%
% of patients gaining >= 0 letters
Macugen: 33% Placebo: 23%
% of patients gaining >= 5 letters
Macugen: 22% Placebo: 12%
% of patients gaining >= 10 letters
Macugen: <b>11%</b> Placebo: <b>6%</b>
% of patients gaining >= 15 letters
Macugen: 6% Placebo: 2%
% of patients losing >= 30 letters
Macugen: 10% Placebo: 22%
% of patients having VA <= 20/200
Macugen: 38% Placebo: 56%
Endophthalmitis: 0.16%/injection with 0.1%/pt/yr severe vision loss Retinal detachment: 0.08%/injection Traumatic cataract: 0.07%/injection with 0.1%/pt/yr severe vision loss Others: vitreous floaters, vitreous opacities, anterior chamber inflammation

Although the prespecified primary endpoint was set to be 54 weeks, the study continued over two years. The second year of the study was designed to assess the need for continued treatment beyond one year and included 1,053 patients. The study demonstrated that 59% of those on Macugen lost less than three lines versus 45% in the sham group. In addition, patients who discontinued treatment with Macugen after one year experienced more VA deterioration than

those who continued on Macugen injections. Therefore, Eyetech is positioning the drug as a twoyear therapy to achieve maximal benefits.

### **IP** Position

Eyetech has an exclusive, worldwide license from Gilead Sciences and its subsidiary NeXstar Pharmaceuticals related to the development, manufacture, and commercialization of products containing Macugen for all indications. The patents pertaining to this license expire between 2010 and 2017. The company has a license from Nektar Therapeutics related to the PEGylation reagent and the patent rights expire between 2013 and 2016. Eyetech also has a license from Isis Pharmaceuticals related to the production and sale of Macugen worldwide; the patents expire between 2010 and 2014.

### Commercialization

Eyetech entered a collaborative agreement with Pfizer for Macugen in December 2002. Pfizer initially paid Eyetech \$100 million (\$75 million up-front license fee and \$25 million equity investment). Pfizer has funded, and will continue to fund the majority of the development costs for Macugen in AMD and other indications. In the United States, Macugen was approved in December 2004 and was launched in January 2005 with a price of \$995 per injection. It will be co-promoted by the two companies, and Eyetech will book Macugen sales in the United States and will share profits from Macugen sales on a 50/50 basis with Pfizer. Outside the United States, Pfizer will commercialize Macugen and pay Eyetech a royalty on net sales. The EMEA, the European regulatory authority, accepted Macugen's marketing authorization application in September 2004. In our model, we assume that Macugen will be approved in Europe in 4Q:05 and will be commercialized in 1Q:06. In addition, Eyetech is eligible to receive up to \$450 million in milestone payments from Pfizer based on prespecified levels of Macugen sales. The effective life of this agreement is around 15 years.

There are approximately 1,400 retinal specialists in the United States who are the target audience for Macugen. Eyetech will use its own 60-person field sales force to detail to these physicians, in addition to Pfizer's 160 reps who will add to the effort and detail to general ophthalmologists.

### Competition

### **Current Treatment Options**

There is no cure for wet AMD at present and available treatments have limited therapeutic benefits.

- Laser Photocoagulation: As the best studied of all current therapies, laser ablation of CNV lesions is the only treatment with proven long-term (five years) benefit in preserving vision, as shown by the Macular Photocoagulation Study (MPS). However, three major limitations restrict the use of thermal lasers in treating wet AMD: 1) only about 10% to 15% of all lesions are small enough and sufficiently defined on angiography (i.e., classic lesions) to be eligible; 2) there is at least a 50% chance of recurrence in the treated eye two years following treatment; and 3) the laser treatment irreversibly destroys the retina and causes a permanent corresponding blind spot; therefore, patients treated for subfoveal lesions experience immediate loss of central vision, although the extent of vision loss is less than in untreated eyes with long-term follow-up. As a result, laser photocoagulation is primarily reserved for CNV lesions away from the fovea.
- **Photodynamic therapy:** PDT for the treatment of wet AMD involves the intravenous infusion of a photosensitizer, such as Visudyne, that preferentially binds to CNV followed by the application of a non-thermal laser light to the retina to selectively destroy the CNV. The treatment is ideally given once every three months, as needed for leakage seen on

angiography. The greatest amount of benefit from PDT is seen in patients with the predominantly classic form of wet AMD. However, recent treatment guidelines recommend PDT with Visudyne for not only predominantly classic CNV but also small [less than or equal to four disc areas (DA)] occult and minimally classic CNV that are progressing. In the United States, PDT with Visudyne is only approved for the treatment of predominantly classic CNV, but is also reimbursed for the treatment of certain occult and minimally classic lesions (i.e., those with recent disease progression and a lesion size less than or equal to four DA). In many countries outside the United States, PDT with Visudyne is approved for one or more types of wet AMD. An average of six treatments of PDT with Visudyne is usually required over a period of two years. In the pivotal TAP trials, after 12 months 61% of treated patients versus 46% in the placebo group lost fewer than three lines. The mean change in visual acuity from baseline was -2.2 lines in the treatment group versus -3.5 lines in the placebo group. For the percentage of patients who 1) gained three or more lines, and 2) gained zero or more lines, PDT with Visudyne showed benefit: 1) 6% of treated patients versus 2% of placebo group, and 2) 38% versus 24%. Many physicians have found that when PDT is combined with intravitreal injections of triamcinolone, a steroid not approved by the FDA for intraocular usage, the therapeutic results are more promising than with PDT alone. Multiple studies are under way to better define the potential of this combination. PDT with Visudyne is generally well tolerated; adverse events include visual disturbances (18%), vitreous hemorrhage (1%), injection site events (13%), infusion-related back pain (2%), allergic reactions (1%), and photosensitivity reactions (3%).

#### **Products in Late-Stage Development**

Wet AMD has become a therapeutic focus for many biotechnology and pharmaceutical companies in recent years. Several late-stage compounds for the treatment of wet AMD are listed below:

Lucentis is a humanized monoclonal antibody fragment targeting all isoforms of VEGF delivered also via intravitreal injections. Lucentis has shown promising results in early stage clinical trials.

EXHIBIT		Lucentis (rhuFab v2, ranibizumab)
<b>3:</b> Lucentis Phase Ib/II in AMD		rhuFabV2 (an Anti-VEGF Antibody Fragment) in Neovascular AMD: Safety and Tolerability of
Source: Company Report and		Multiple Intravitreal Injections
First Albany Capital		Phase Ib/II
T itsi Mouty Capital	Study Design	Open-label, randomized, controlled, multi-center, 64 patients
		Randomized to Lucentis 300 µg; 500 µg; "usual care"
		Injection Q 28 days x 4; subjects may cross over for 12 weeks after initial study period
	Patient Demographics	Average age: 77
		Median baseline VA: 20/125 (range 20/50 - 20/500)
		Predominantly classic (33%), minimally classic (39%), active lesion post-PDT (28%)
	Primary Endpoint	Visual acuity (ETDRS) at day 210
	Efficacy	% of patients losing < 15 letters (3 lines)
		94% at day 98, 97% at day 210
		% of patients gaining >= 15 letters
		26% at day 98, 45% at day 210
		Change in visual acuity
		0.3 mg: +7.4 letters at day 98, +12.8 letters at day 210
		0.5 mg: +12.6 letters at day 98, +15.0 letters at day 210
		Usual care: -5.1 letters at day 98
	Adverse Events	Crossover to 0.3 mg at day 98: +7.3 letters from baseline at day 210
		Crossover to 0.5 mg at day 98: +3.2 letters from baseline at day 210
		Transient, asymptomatic inflammation most frequent
		5% severe uveitis, endophthalmitis, and CRVO

We estimate that Lucentis is approximately two years behind Macugen, as it is currently undergoing multiple studies, as shown in Exhibit 4.

EXHIBIT	Study	Design	Status
4: Lucentis Clinical Program Source: First Albany Capital	MARINA	Phase III, double-masked study involving 717 patients with minimally classic or occult wet AMD randomized to receive sham injection, 0.3 mg Lucentis, or 0.5 mg Lucentis.	Enrollment completed year-end 2003 One-year data are expected 2Q:05
	ANCHOR	Phase III, double-masked, active-treatment controlled trial in 426 patients with predominantly classic wet AMD randomized to receive PDT + sham injection, sham PDT + 0.3 mg Lucentis, or sham PDT + 0.5 mg Lucentis.	Enrollment completed October 2004 Data are expected 4Q:05
	FOCUS	Phase Ic, single-masked, open-label study involving 168 patients with predominantl classic wet AMD randomized to receive either Lucentis 0.5 mg plus PDT or sham injection + PDT.	Enrollment completed early 2004 Data are expected 2Q:05
	PIER	Phase IIIb, double-masked, sham-injection controlled study in 180 patients with predominantly classic or occult wet AMD randomized to receive Lucentis or sham injections monthly for three months then once every three months. The purpose of PIER is to help determine the optimal dosing schedule for Lucentis.	Initiated in 3Q:04 Currently enrolling
	PrONTO	Two-year, open-label, uncontrolled study to evaluate durability of response for Lucentis and whether optical coherence tomography (OCT) can be used to guide treatment of wet AMD with Lucentis. OCT is a non-invasive imaging technique similar to ultrasonography but using light waves to obtain high resolution cross-sectional images of the retina.	Ongoing

- Retaane (anecortave acetate, Alcon) is a depot suspension of a steroid delivered as a juxtascleral (next to the back of the eyeball) injection. The drug failed to meet the primary endpoint of non-inferiority to PDT in its pivotal Phase III trial. At one year, 45% of those receiving Retaane maintained vision, defined as less than a three-line loss in VA, compared to 49% in the PDT group. Alcon believes that reflux and therapy interval contributed to the less-than-ideal results. Retaane is currently under FDA review. The FDA decision is expected in late May 2005. In our opinion, the drug is unlikely to be approved until another Phase III study is successfully completed.
- Evizon (squalamine, Genaera) is a small-molecule anti-angiogenesis drug administered via intravenous infusions. Early clinical testing of Evizon in the treatment of wet AMD has also shown promising results. In a Phase I/II clinical trial conducted at a single site in Mexico City, 40 patients with predominantly classic or occult wet AMD were treated with 25 or 50mg/m<sup>2</sup> of Evizon administered intravenously every week for four weeks. Visual acuity was assessed using the ETDRS chart at baseline, four weeks, two months, and four months of the study. At the end of four months, 100% of patients had lost fewer than three lines on the ETDRS chart, one of the main parameters evaluated for efficacy of treatment in AMD. Mean visual acuity improved an average of 1.2 lines (six letters). The median visual acuity improved from 20/125 to 20/100. Furthermore, in two other measures which retina specialists consider—percentage of patients who 1) gained three or more lines, and 2) gained zero or more lines—Evizon showed benefit: 1) 26%, and 2) 100%. Evizon was well tolerated in this trial. Adverse events were mostly related to drug administration—injection site pain and phlebitis. Evizon is currently in multiple Phase II studies and is scheduled to enter pivotal Phase III studies in 2Q:05.

### **Other Indications**

Eyetech is currently pursuing additional ophthalmic indications for Macugen. Diabetic macular edema (DME) is a complication of diabetic retinopathy. The underlying pathology is leakage of the plasma from blood vessels in the macula, leading to severe loss of central vision. There are approximately 500,000 patients with DME in the United States and the incidence is estimated to be about 75,000 cases in the United States each year. In May 2004, Eyetech announced the results from a randomized, double-masked, placebo-controlled, Phase II trial involving 169 patients with DME. At 36 weeks, 73% of patients treated with Macugen 0.3mg gained zero or more lines of

visual acuity compared to 51% in the sham injection group; 59% gained one or more lines in the Macugen 0.3mg arm versus 34% in the sham injection arm; 34% gained two or more lines in the Macugen 0.3mg arm versus 10% in the sham injection arm. All of these results were statistically significant. In addition, optical coherence tomography (OCT) showed that patients treated with Macugen 0.3mg had a substantial reduction in retinal thickness, which is linked to leakage of the abnormal blood vessels, compared to the control group. Eyetech and Pfizer plan to begin a Phase III study for Macugen for the treatment of DME later this year.

Retinal vein occlusion (RVO) is believed to be the most common retinal vascular disorder in the United States. It is classified into ischemic and non-ischemic types and has a multi-factorial pathogenesis. The ischemic type has a very poor prognosis for visual acuity; the non-ischemic type has a comparatively more benign prognosis. Photocoagulation is the current treatment of choice, but has limited efficacy. Eyetech began a Phase II trial in May 2004 to evaluate the efficacy and safety of Macugen in treating this disorder, which is characterized by high VEGF levels. From 50 to 100 patients will be enrolled and treated for 12 to 30 weeks. This trial is still enrolling patients and endpoints include change in visual acuity and change in retinal thickness.

### EXHIBIT

5: Macugen's Ongoing and Future Studies Source: First Albany Capital

Study	Status
Combination trial (Macugen + PDT versus Macugen in predominantly classic patients)	Initiation in 2Q:05
DME phase III trial	Initiation in 2005
RVO phase II trial	Enrolling
Early lesion trial	Initiation in 2005
Optical coherence tomography biomarker trial	Initiation in 2005?
Low dose trial	Initiation in 2005-2006
Electroretinography (ERG) trial	Initiation in 2005-2006
Corneal endothelial cell count trial	Initiation in 2005-2006

Name	Position	Position Held Since	Career Highlights/Background
John P. McLaughlin	Chairman of the Board of Directors	Feb. 2000	-President and Chief Executive Officer of Corgentech, Inc     -President of Tularik, Inc. from 1997-1999     -Executive Vice President at Genentech     -coursel to the U.S. House of Representatives committee responsible for     drafting several of the FDA laws
David R. Guyer, M.D.	Chief Executive Officer and Director, Co-founder	Feb. 2000	<ul> <li>-Voluntary Clinical Professor of Ophthalmology at New York University School of Medicine (current)</li> <li>-Chief medical editor of Ophthalmology Times from 1996-present</li> <li>-Professor and Chairman of Dept of Ophthalmology at NYU School of Medicine from 2000-2002</li> <li>-Study Co-chairman of the Pharmacological Therapy for Macular Degeneration Study Group</li> </ul>
Paul G. Chaney	Chief Operating Officer	Aug. 2003	<ul> <li>-Vice President, Global Commercial Operations, Ophthalmology Franchise at Pharmacia Corporation from 2002-2003</li> <li>-Vice President, Global Ophthalmology Business at Pharmacia Corporation from 2001-2002</li> <li>-Vice President, Global Pharmaceutical Ophthalmology at Pharmacia Corporation from 2000-2001</li> <li>-Business Director, Ophthalmology, North America at Pharmacia Corporation from 1998-2000</li> <li>-Director, U.S. Ophthalmology Business at Pharmacia Corporation from 1996-1998</li> </ul>
Glenn P. Sblendorio	Chief Financial Officer and Senior Vice President, Finance	Feb. 2002	<ul> <li>-Senior Vice President of Business Development for The Medicines Company from 2000-2002</li> <li>-Chief Executive Officer, Chief Financial Officer and Managing Director of MPM Capital Advisors, LLC from 1998-2000</li> </ul>
Anthony P. Adamis, M.D.	Executive Vice President, Research/Chief Scientific Officer, Co-founder	July 2002	<ul> <li>-Associate Professor of Ophthalmology at Harvard Medical School from 1998-2002</li> <li>-Director of Residency Training in Ophthalmology at the Massachusetts Eye and Ear Infirmary from 1992-2002</li> <li>-principal investigator and co-director of the Retina Research Institute for Diabetic Retinopathy and Macular Degeneration at the Massachusetts Eye and Ear Infirmary</li> </ul>
Douglas H. Altschuler	Senior Vice Preseident, Legal, General Counsel and Secretary	May 2003	-General Counsel of Nektar Therapeutics from 2001-2003 -General Counsel of Axys Pharmaceuticals from 2000-2001 -Vice President/General Counsel and Compliance Officer of Mentor Corporation from 1996-2000

## **Senior Management**

EXHIBIT 6: Senior Management Source: Company report

## FINANCIAL OVERVIEW

Eyetech reported a net loss of \$29.8 million, or \$0.72 per share, in 4Q:04. The company had \$11.6 million in collaboration revenue related to the Pfizer agreement for Macugen. Eyetech had \$211.5 million in cash and cash equivalents at the end of December 2004. In addition, the company received \$90 million from Pfizer for obtaining FDA approval for Macugen in January 2005. We project that the company will become profitable in 2006.

### **Financial Models**

### EXHIBIT

7: Income Statement Source: Company report and First Albany Capital

### Eyetech Pharmaceuticals, Inc.

#### **Income Statement**

(\$ in thousands, except per-share amounts)

	2003A	2004A	Mar-05	Jun-05	Sep-05	Dec-05	2005E	2006E	2007E	2008E
For years ending December 31:	Annual	Annual	1Q05E	2Q05E	3Q05E	4Q05E	Annual	Annual	Annual	Annual
Revenues:										
Macugen U.S. Sales			22,149	34,574	43,218	51,862	151,803	406,498	402,747	387,621
Macugen ex-U.S. Royalty								17,078	45,731	45,309
Collaboration Revenue	41,419	49,352	12,125	12,425	12,725	13,025	50,300	59,630	61,552	63,569
Total revenues	41,419	49,352	34,274	46,999	55,943	64,887	202,103	483,206	510,030	496,499
Costs and expenses:										
Cost of Goods Sold			5,537	8,644	10,804	12,965	37,951	101,625	100,687	96,905
Payment to Pfizer for U.S. Macugen Sales			8,306	12,965	16,207	19,448	56,926	152,437	151,030	145,358
Research and Development	70,932	102,739	14,500	15,000	15,500	16,000	61,000	64,050	67,253	70,615
Sales and Marketing	4,599	33,343	11,000	10,000	10,000	11,000	42,000	38,000	34,000	30,000
General and Administrative	6,823	17,435	8,000	8,125	8,250	8,500	32,875	34,519	36,245	38,057
Total costs and expenses	82,353	153,517	47,343	54,734	60,761	67,913	230,752	390,630	389,214	380,935
Operating income (loss)	(40,934)	(104,165)	(13,069)	(7,735)	(4,818)	(3,027)	(28,649)	92,576	120,816	115,564
Interest income (expense)	1,923	3,659	1,150	1,000	1,000	1,000	4,150	4,250	4,500	5,000
Other										
Pretax income (loss)	(39,011)	(100,506)	(11,919)	(6,735)	(3,818)	(2,027)	(24,499)	96,826	125,316	120,564
Income taxes (benefit)	(1,688)							36,794	47,620	45,814
	,							38%	38%	38%
Preferred stock accretion and Other	(9,160)	(816)								
Net income (loss)	(49,860)	(101,322)	(11,919)	(6,735)	(3,818)	(2,027)	(24,499)	60,032	77,696	74,750
EPS (basic)	(\$1.77)	(\$2.56)	(\$0.28)	(\$0.16)	(\$0.09)	(\$0.05)	(\$0.57)	\$1.30	\$1.56	\$1.40
EPS (diluted)	(\$1.77)	(\$2.56)	(\$0.28)	(\$0.16)	(\$0.09)	(\$0.05)	(\$0.57)	\$1.23	\$1.49	\$1.33
Basic Shares	28,094	39,651	42,120	42,752	43,394	44,044	43,078	46,309	49,782	53,515
Diluted Shares	28,094	39,651	42,120	42,752	43,394	44,044	43,078	48,624	52,271	56,191

### EXHIBIT

8: Balance Sheet

Source: Company report and First Albany Capital

Balance Sheet						
(Dollars in thousands)						
For years ending December 31:	2003A	2004A	2005E	2006E	2007E	2008E
Assets						
Cash & Equivalents	131,374	211,495	158,033	196,361	288,286	372,482
Prepaids and Other Current Assets	3,863	99,834	119,801	143,761	172,513	207,016
Total Current Assets	135,237	311,329	277,834	340,122	460,799	579,498
Property and Equipment, net	5,868	17,817	32,856	50,903	72,559	98,546
Other assets	8,375	10,313	11,859	13,638	15,684	18,037
Total Assets	149,480	339,459	322,549	404,663	549,041	696,080
Liabilities and Shareholders' Equity Accounts Payable and Accrued Expenses	14,308	25,103	30,124	36,149	43,378	52,054
	14,308 5,790	25,103 16,191	30,124 18,215	36,149 20,492	43,378 23,053	52,054 25,935
Accounts Payable and Accrued Expenses	,	,		,	,	,
Accounts Payable and Accrued Expenses Deferred Revenue and Other Current	5,790	16,191	18,215	20,492	23,053	25,935
Accounts Payable and Accrued Expenses Deferred Revenue and Other Current Total current liabilities	5,790 20,098	16,191 41,294	18,215	20,492	23,053	25,935
Accounts Payable and Accrued Expenses Deferred Revenue and Other Current Total current liabilities Long-term Debt	5,790 20,098 1,038	16,191 41,294 1,255	<u>18,215</u> 48,339	20,492 56,640	23,053 66,431	25,935 77,989 242,707
Accounts Payable and Accrued Expenses Deferred Revenue and Other Current Total current liabilities Long-term Debt Other Liabilities	5,790 20,098 1,038 65,842	16,191 41,294 1,255 165,772	18,215 48,339 182,349	20,492 56,640 200,584	23,053 66,431 220,643	25,935 77,989

### EXHIBIT

9: Statement of Cash Flows

Source: Company report and First Albany Capital

Eyetech Pharmaceuticals, Inc.						
Cash flow						
(Dollars in thousands)						
For years ending December 31:	2003A	2004A	2005E	2006E	2007E	2008E
Cash flows from operating activities:						
Net income/ (loss)	(40,699)	(100,506)	(24,499)	60,032	77,696	74,750
Depreciation & amortization	891	2,196	2,745	3,431	4,289	5,361
Other adjustments	4,756	12,313	14,161	16,285	18,727	21,536
Changes in working capital	74,492	19,482	(22,405)	(25,765)	(29,630)	(34,075)
<b>Operating Cash Flow</b>	39,441	(66,514)	(29,998)	53,982	71,082	67,572
Cash flows from investing activities:						
Capital expenditures	(3,778)	(12,532)	(15,039)	(18,047)	(21,656)	(25,987)
Other	(48,153)	(65,438)	80,000	40,000	40,000	40,000
Investing Cash Flow	(51,931)	(77,971)	64,961	21,953	18,344	14,013
Cash flows from financing activities:						
Stock issuance (buy-back), net	250	158,308	250	250	250	250
Debt issuance (payment), net		,				
Other	31,463	1,943	2,040	2,142	2,249	2,362
Financing Cash Flow	31,712	160,251	2,290	2,392	2,499	2,612
Net change in cash	19,222	15,766	37,253	78,328	91,925	84,197
Cash at beginning of year	5,792	25,014	40,780	78,033	156,361	248,286
Cash at year end	25,014	40,780	78,033	156,361	248,286	332,482

### PUBLIC COMPANIES MENTIONED IN THIS REPORT:

Alcon Inc. (ACL - \$88.85 - Not Rated) Genaera Corp. (GENR - \$2.40 - Neutral) Genentech Inc. (DNA - \$57.08 - Buy) Gilead Sciences Inc. (GILD - \$35.86 - Not Rated) Isis Pharmaceuticals Inc. (ISIS - \$3.93 - Not Rated) Nektar Therapeutics (NKTR - \$14.11 - Not Rated) Pfizer Inc. (PFE - \$26.29 - Neutral) QLT Inc. (QLTI - \$12.76 - Buy)

Stocks priced as of March 30, 2005

### **Regulation AC Disclosure:**

Each analyst and associate who has participated in the preparation of this report certifies that the views expressed in this publication accurately reflect the personal views of the analyst about the subject company(s) and its (their) securities. The analyst and associate further certify that they have not received and will not be receiving direct or indirect compensation in exchange for expressing the recommendation contained in this publication.

### **Required Disclosures:**

First Albany Capital makes a market in the securities of QLT.

### First Albany Capital's Rating System

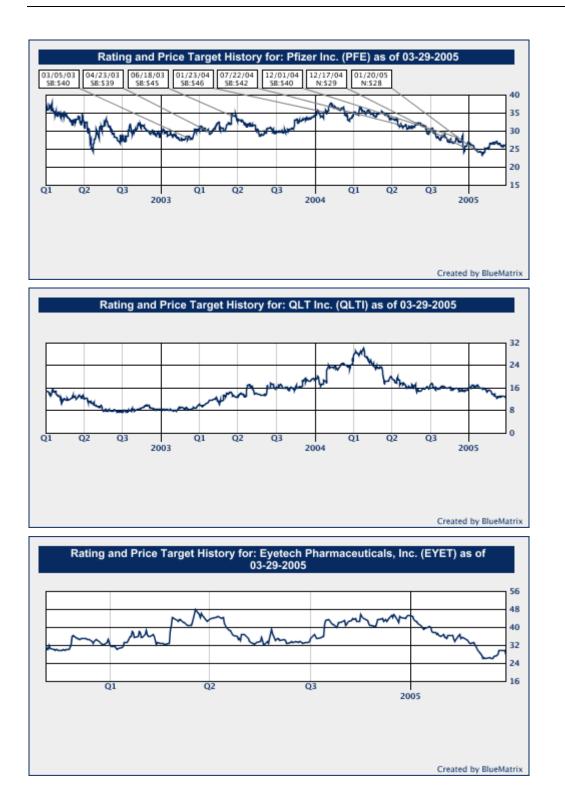
Strong Buy—Potential return of 20% or more.
Buy—Potential return of 10%-20%.
Neutral—Fairly valued.
Underperform—Negative potential return of 10%-20%.
Sell—Negative potential return of 20% or more.
Restricted— Applicable laws and regulations preclude certain types of communications during the course of First Albany Capital's engagement in investment banking transaction and in certain other circumstances

Quarterly Report for 3/30/2005

Entire Universe - To	otal: 248			
	Buys: 140(56.5%)	Sells: 10(4%)	Holds: 94(37.9%)	
Banking Client Univ	verse - Total: 29			
	Buys: 20(68.8%)	Sells: 0(0%)	Holds: 9(30.9%)	
Entire Universe By	Vertical - Total: 248			
Consumer	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Economics	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Energy	Buys: 28(11.3%)	Sells: 1( 0.4%)	Holds: 23( 9.3%)	Total: 53
Equity Research	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Fixed Income	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Healthcare	Buys: 56(22.6%)	Sells: 2( 0.8%)	Holds: 34(13.7%)	Total: 95
Special Situations	Buys: 16( 6.5%)	Sells: 0( 0.0%)	Holds: 4( 1.6%)	Total: 20
Technology	Buys: 40(16.1%)	Sells: 7( 2.8%)	Holds: 33(13.3%)	Total: 80
Banking Client Univ	verse By Vertical - T	otal: 29		
Consumer	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Economics	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Energy	Buys: 5(17.2%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 5
Equity Research	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Fixed Income	Buys: 0( 0.0%)	Sells: 0( 0.0%)	Holds: 0( 0.0%)	Total: 0
Healthcare	Buys: 11(37.9%)	Sells: 0( 0.0%)	Holds: 5(17.2%)	Total: 16
Special Situations	Buys: 1( 3.4%)	Sells: 0( 0.0%)	Holds: 1( 3.4%)	Total: 2
Technology	Buys: 3(10.3%)	Sells: 0( 0.0%)	Holds: 3(10.3%)	Total: 6



2003 2004 2005 01/11/05 N:\$51 10/09/03 10/28/03 SB:\$43 SB:\$45 12/23/03 SB:\$54.5 01/15/04 SB:\$56 04/08/04 S8:\$58 04/26/04 S8:\$64 07/08/04 BY:\$63 03/15/05 N:\$59 03/21/05 BY:\$63 Created by BlueMatrix



For our latest pricing chart for any of the companies mentioned in this report for which First Albany has maintained a rating for more than one year, depicting price target and rating revisions, please refer to <a href="http://www.firstalbany.com/download3.asp?categoryID=180">http://www.firstalbany.com/download3.asp?categoryID=180</a>

### **Other Disclosures and Disclaimers:**

Although not compensated directly for any banking deals, an analyst may receive income from a bonus pool that may include monies derived from banking revenues.

Blue Sky exception in VI for QLT.

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# EQUITY RESEARCH DEPARTMENT

Christina Rizopoulos V	alauri, Director of Research	(212) 273-7201
	Energy	
	Diversified Industrials/Energy Technology	
	Sanjay Shrestha	(212) 273-7186
	Craig Irwin	
	Stephen DeNichlio, CFA – Associate	
	Exploration & Production	( )
	David R. Tameron	
	Oilfield Equipment and Services	(
	R. Thaddeus Vayda	(212) 273-7221
	Healthcare	(_ · _) _ · 0 · ·
	Biotechnology	(242) 272 7453
	David Webber	
	Biotechnology	(040) 070 7400
	Lucy Lu	
	Healthcare Services	(04.0) 070 74.00
	Glenn Garmont	
	Christine Meany – Associate	
	Medical Technology	
	William J. Plovanic, CFA	
	Brian Wong – Associate	
	Medical Technology/Devices	
	Jason R. Mills	(415) 262-5012
	Specialty Drugs/Major Pharmaceuticals	
	Adam Greene	( )
	Michael Assenza – Associate	(212) 273-7121
	Technology	
	Enterprise Application Software	
	Mark R. Murphy	
	Jordan Welu – Associate	
	Infrastructure Software	
	Scott Zeller	( )
	Andrew Fernandez, CFA – Associate	
	Internet and New Media	
	Jason Avilio	
	IT Hardware & Storage Infrastructure	
	Joel Wagonfeld	(415) 262-5054
	Alice Akahoshi – Associate	(415) 262-5029
	Semiconductor Components & Capital Equipment	
	Gus Richard, CFA	(415) 262-5005
	Telecom Services and Equipment	
	Frank Marsala, CFA	
	Santosh Rao – Associate	(212) 273-7114
	Special Situations	
	Randall Scherago	(115) 262 5055



# EQUITY CAPITAL MARKETS INSTITUTIONAL SALES OFFICES

#### Boston

First Albany Capital 100 Federal Street Boston, Massachusetts 02110 800 541-5062

#### Chicago First Albany Capital

29 North Wacker Drive Chicago, Illinois 60606 877 751-2820

#### Minneapolis

First Albany Capital 294 East Grove Lane Wayzata, Minnesota 55391 877 925-3220

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First Albany Capital One Penn Plaza New York, New York 10119 800 228-1146

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