William Blair

Avalanche Biotechnologies, Inc.

Eyeing the Next Disruption in the AMD Market; Initiating Coverage With Outperform Rating and $52 Price Target

Avalanche Biotechnologies is a potentially disruptive company in the eye care market. Its lead drug, AVA-101, is in a Phase IIa study set to report data in the first half of 2015—data that could signal a significant step forward in the $3 billion domestic and larger international market for the treatment of wet age-related macular degeneration (wet AMD). AVA-101 is a gene therapy–based treatment that aims to be a curative therapy for wet AMD, a disease for which two VEGF-targeting therapies, Eylea from Regeneron and Lucentis from Genentech, are already blockbuster brands.

While AVA-101 is early in development and still holds significant clinical risk, we believe shares of Avalanche hold an asymmetric risk/reward given the potential to transform the AMD, diabetic macular edema (DME), and retinal vein occlusion (RVO) markets. We believe Eylea, with sales annualizing to over $1.6 billion, has proved the power of reduced dosing, and a curative therapy would obviously be disruptive in the market.

AVA-101 is delivered through a subretinal injection that introduces the sFlt-1 gene, a naturally occurring potent VEGF inhibitor. We believe the Phase I data is strong; four out of six patients treated with AVA-101 were functionally cured over 52 weeks and did not need Lucentis injections, while two patients treated with AVA-101 required only one injection over 52 weeks. Treated subjects on average required only 0.33 Lucentis injections over 52 weeks, suggesting a significant treatment effect, albeit in a small number of patients. Based on data to date, we believe the Phase IIa results, due in early 2015, should be a significant catalyst for shares. Avalanche is also developing pipeline products based on proprietary ocular-based AAV technology to be applied to dry AMD and other rare eye diseases. We view the $640 million development partnership and equity investment by Regeneron as another validation of gene therapy potential in ophthalmic diseases.

Based on the asymmetric risk/reward for lead program AVA-101, we are initiating coverage of Avalanche with an Outperform rating. Our $52 price target is derived from our NPV model for AVA-101. Given the early stage, we are taking a risk adjustment of a 50% probability of success. However, if AVA-101 continues to look like a curative therapy in AMD in the Phase IIa study, our price target is likely conservative. With Avalanche's ocular-focused gene therapy platform and developing pipeline, we believe it will join the ranks of other midcap biotechnology companies pending a positive readout. As Avalanche is in the early stages of developing AVA-101 and its ocular gene therapy candidates, risks to investing are primarily clinical and regulatory in nature.

Avalanche Biotechnologies is a biotechnology company located in Menlo Park, California, focused on developing gene-based therapies for the treatment of ocular diseases.

August 25, 2014
Basic Report (14-109)

Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$52
Symbol:	AAVL (NASDAQ)
Price:	$30.15 (52-Wk.: $22–$32)
Market Value (mil.):	$644
Fiscal Year End:	December

Estimates	**2013A**	**2014E**	**2015E**
EPS FY	-$1.44	-$0.37	-$0.97
EBITDA (mil.)	-$2.63	-$11.72	-$22.33
Valuation			
P/E	NM	NM	NM

Trading Data	
Shares Outstanding (mil.)	21.36
Float	53%
Average Daily Volume	539,999

Financial Data	
Long-Term Debt/Total Capital	NM
Book Value Per Share	NM
Enterprise Value (mil.)	$494
EBITDA (mil.)	-$2.63
Enterprise Value/EBITDA	NM

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Company Overview

Avalanche Biotechnologies is focused on the development of ocular gene therapy products that have the potential to provide curable treatments for sight-threatening diseases. The company's lead product, AVA-101, is a gene therapy–based product that works by inhibiting vascular endothelial growth factor (VEGF), the same target as Lucentis and Eylea, two products that have transformed the treatment of wet age-related macular degeneration (AMD).

The company has produced compelling early data to date from a Phase I placebo-controlled study in which the six patients were treated with AVA-101, requiring an average of 0.33 injections out of 12 opportunities. Despite the small number of patients, the trial reached a statistically significant efficacy result compared with a Lucentis control group as well as a historical control ($P < 0.001$). All patients entering the Phase I study had been heavy users of Lucentis before treatment with AVA-101. Based on the results observed in the company's Phase I placebo-controlled study, Avalanche initiated a Phase IIa study based in Australia, which will read out results in early 2015. If the Phase IIa trial shows efficacy approaching what has been observed in the company's small Phase I trial, we believe AVA-101 will become one of the most strategically valuable assets in the sector. And while we believe partnership interest will be significant given the successful franchises built in AMD over the past decade at Roche/Genentech and Regeneron, we would not be surprised if the company were to attempt to retain U.S. rights and develop the product itself.

In addition to AVA-101, Avalanche is advancing a portfolio of therapies targeting rare ophthalmic diseases with severe outcomes. And while gene therapy has had false starts in the past, we note that several academic groups have recently had success in gene therapy—more specifically, in gene therapy to treat ophthalmic indications. In total, we believe management has chosen its indications appropriately, with all weighing heavily toward a favorable risk/reward for treatment given the lack of other therapies and the severity of the diseases.

We are also not the only ones excited about the Avalanche platform's potential, as the company recently signed a large partnership with AMD leader Regeneron. The partnership includes an up-front payment and Regeneron also took an equity stake through participation in Avalanche's initial public offering. We see this participation by a leader in AMD as a validation of the potential opportunity for Avalanche. We also note that several leaders in the rare disease space, including Sanofi and BioMarin, have started to invest in gene therapy. Also, with the European approval of uniQure's gene therapy product, Glybera, the regulatory pathway might not hold as much risk as investors tend to believe. Given the potential for AVA-101 as well as the company's platform of ocular-specific gene therapy targets, we are initiating coverage of Avalanche with an Outperform rating and Aggressive Growth profile. Our net-present-value (NPV) model for AVA-101 alone suggests $52 per share in value, despite a 50% probability of success adjustment given the early stage of development and numerous regulatory and clinical hurdles in developing a new technology such as gene therapy. We include the relevant timeline-and-events and pipeline summaries for Avalanche in exhibits 1 and 2, on the following page.

Exhibit 1
Avalanche Biotechnologies, Inc.
Timeline and Events

Date	Product	Event	Description/Comments
2014			
Sept 11 to 14	AAV2-sFLT01	Conference	Retina Society Meeting in Philadelphia, PA (Sanofi/AGTC data)
Oct 18 to 21	Wet AMD candidates	Conference	American Academy of Opthalmology Annual Meeting in Chicago, IL
2015			
H1 2015	AVA-101	Clinical	Phase IIa readout
H2 2015	AVA-101	Clinical	Initiate Phase IIb study (N=120)
H2 2015	AVA-101	Regulatory	IND filing
2015	AVA-201	Clinical	Preclinical studies
2015	AAV2-sFLT01	Clinical	Phase I readout of Sanofi/AGTC product
2016			
2016	Multiple	Regulatory	IND filings of other product candidates
2016/2017	AVA-101	Clinical	Potential initiation of pivotal program

Sources: Company reports and William Blair & Company, L.L.C. estimates

Exhibit 2
Avalanche Biotechnologies, Inc.
Current Product Pipeline

Drug Candidate	Research/ Preclinical	Phase I	Phase II	Phase III/ Pivotal	NDA/MAA Filing	Comments/Timing
AVA-101						Wet AMD, Exclusive Worldwide Rights, Phase IIa Readout in 1H 2015
AVA-101						Diabetic Macular Edema/Retinal Vein Occlusion, Exclusive Worldwide Rights
AVA-201						Wet AMD Prevention, Exclusive Worldwide Rights
AVA-311						Juvenile X-Linked Retinoschisis, Partnered
AVA-322/AVA-323						Undisclosed Orphan Target, Exclusive Worldwide Rights

Sources: Company reports and William Blair & Company, L.L.C.

Key Risks

Clinical risks in developing a new cutting-edge technology. Past attempts at gene therapy, taken in the 1990s, led to significant failures that dampened enthusiasm for the technology. Any clinical or regulatory setbacks for the AVA-101 program or other gene therapy products in development by the other programs in the clinic would weigh heavily on company shares.

As Avalanche ramps up manufacturing, commercial-scale manufacturing risk remains. The company is scaling manufacturing of AVA-101 through its partner Lonza Group, a leader in the manufacturing of biologic therapies. While gene therapy is a novel technology, we believe the company will be able to leverage the extensive manufacturing expertise that has been developed in the vaccine industry as the company needs to scale.

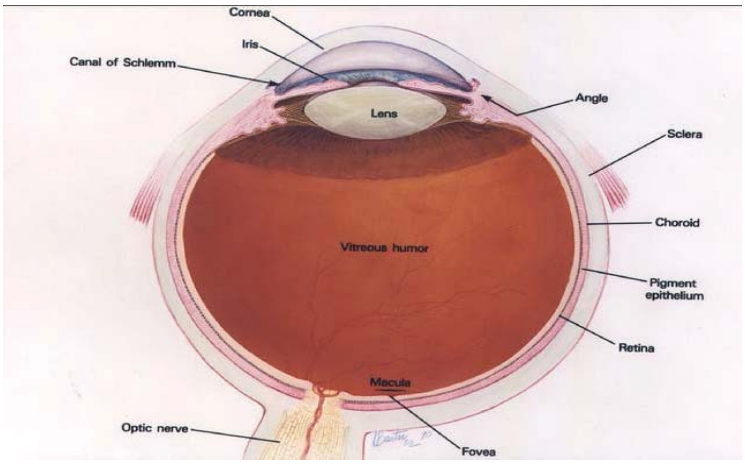
The company faces the clinical and regulatory risks typical of a development-stage therapeutics company. There is limited patient experience with AVA-101, with only Phase I data produced to date. This study included only six patients on active therapy, although the inclusion of a placebo control produced higher-quality data than what is normally observed in early-stage studies. However, given the limited number of patients treated to date with AVA-101, clinical risk remains as the company enrolls its Phase IIa study.

Eye Anatomy Overview

To understand the mechanism of AVA-101 and how it affects wet AMD, we must first describe some basic eye anatomy. As shown in exhibit 3, the most superficial part of the eye includes the cornea, iris, and lens. Behind this is the vitreous body, which contains a jelly-like substance and separates the lens and the retina. The macula is the part of the eye that is near the center of the retina, and the central pit of the macula is called the fovea. Light that enters the eye is focused primarily by the cornea, and the iris of the eye controls the amount of light that can reach the back of the eye by adjusting pupil size. The lens helps the eye automatically focus on near and approaching objects.

The light that is controlled and focused reaches the retina, a 10-layered inner eye lining at the back of the eyeball. The two outer layers contain the light-sensitive rod and cone photoreceptor cells supported by Muller cells, which are embedded in the interphotoreceptor matrix and in close contact with the retinal pigment epithelium (RPE). The RPE is surrounded by two extracellular matrices, the interphotoreceptor matrix, and Bruch's membrane. Between the RPE and the sclera (or outer wall of the eye) are Bruch's membrane, the choriocapillaris, and the choroid (a larger vessel layer).

Exhibit 3
Avalanche Biotechnologies, Inc.
Eye Anatomy



Source: National Eye Institute

The RPE is a phagocytic system essential to the renewal of photoreceptors. Each photoreceptor has inner and outer segments; the outer segment of each rod has roughly 1,000 discs, and the outer segment of each cone has a membrane that is folded 700 times. Discs are necessary for the conversion of light into electric potentials. Each disc membrane has rhodopsin, a transmembrane protein, in combination with four phospholipids and docosahexaenoic acid. The renewal of the photoreceptors occurs with the addition of membranes at the base of the outer segments of rods and the replacement of building blocks throughout the cones. RPE and photoreceptor health are critical to visual health; when they are degraded and unable to be replenished, ocular diseases result.

Background on Retina Diseases Treated With VEGF Inhibition

Age-Related Macular Degeneration Represents a Significant Health Concern

Age-related macular degeneration (AMD) is a progressive retinal disease that usually occurs in patients 55 and older. According to the BrightFocus Foundation (a nonprofit that supports research and education of brain and eye diseases), as many as 11 million people in the United States have some form of macular degeneration; this number is expected to double by 2050. In addition, more than 2 million Americans live with the most advanced form of the disease. The disease is stratified in early and late stages; the early stage is usually referred to as the dry form of the disease, whereas the late stage is referred to as the wet form. According to AMD Alliance International, dry AMD accounts for 85% to 90% of all cases and is characterized by good vision and the presence of drusen (small, round, white-yellow fatty deposits in the macula) and/or pigment epithelial changes with a risk of progression of the disease. The amount of vision loss is correlated to the location and amount of macular thinning caused by the drusen, which can accumulate under the retina between the retinal pigmented epithelium layer and Bruch's membrane, which supports the retina. Over time, drusen are associated with the deterioration of the macula and the death of RPE and photoreceptor cells, leading to blurred vision. Dry macular degeneration can be further segregated into early, intermediate, and advanced stages, depending on the size and quantity of drusen as well as the degree of vision loss.

Wet AMD occurs when abnormal blood vessels grow behind the macula as RPE and photoreceptor cells die. The Bruch's membrane breaks down near drusen deposits and new blood vessels grow in a process known as neovascularization. The new vessels can also leak fluid and blood, which results in the scarring of the macula. It is from this leaking that "wet" AMD receives its name. At this stage, vision can become severely distorted or lost entirely within a short period. According to AMD Alliance and the BrightFocus Foundation, wet AMD accounts for roughly 10% to 15% of AMD cases. However, despite it representing a lower percentage of AMD cases, late AMD is the most common cause of untreatable blindness, with a prevalence of 0.05% before the age of 50 and 11.8% after the age of 80 (Friedman et al. *Arch Ophthalmol* 2004).

Further distinction in wet AMD: classic versus occult forms. The progression of wet AMD can be further divided into two categories—classic and occult—based on the type of choroidal neovascularization (CNV) or underlying process causing abnormal blood vessel growth in an attempt to create a new network of blood flow to supply nutrients and oxygen to the retina. In pure classic CNV, the blood vessels that are involved can be seen distinctly. In the pure occult form, it is impossible to locate the leaking vessels. According to the National Eye Institute, patients often present a combination of both occult and classic CNV, with a portion of the vessels showing a defined site of leakage and another portion of the vessels being obscured. Wet AMD can be classified as predominantly classic if the classic component makes up more than 50% of the entire lesion (less than 50% occult) or minimally classic if the classic component is less than 50% of the entire lesion (more than 50% occult). These distinctions have been thought to play a role in the efficacy of therapy.

Diabetic Macular Edema Is a Growing Cause of Vision Loss, Primarily Because of the Expected Increases in the Global and U.S. Diabetes Populations

Diabetic macular edema (DME) is an ocular complication of type 1 and type 2 diabetes mellitus. It occurs when diabetes, similar to its detrimental effect on other areas of vasculature, causes capillaries in the eye to become abnormally permeable and leak fluid into the retina tissue of the macula of the eye. The result of this can be vision loss and eventual blindness. According to published sources, DME is likely to increase in prevalence along with the increase in diabetes, which is expected to rise more than 50% globally between 2000 and 2030. The number of diabetes cases is estimated to reach roughly 300 million globally by 2025 (King et al. *Diabetes Care* 1998, Wild et al. *Diabetes Care* 2004). In the United States, diabetes affects roughly 8% of the population, or 23.6 million people, and is the leading cause of new cases of blindness, with a projected 12,000 to 24,000 new cases in adults each year (Chen et al. *Curr Med Res Opin* 2010).

The largest epidemiological study of DME in the United States was the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR). The study showed a direct relationship between the prevalence of DME and duration since diabetes diagnosis. Prevalence was zero in younger-onset patients with diabetes for fewer than five years and 29% in younger-onset patients (typically type 1 diabetes) with diabetes for 20 years or more. Among older-onset patients (typically type 2 diabetes), prevalence ranges from 3% to 28%, corresponding with the duration. DME was also more prevalent among insulin users, likely with more severe diabetes, than among non-insulin users; DME was present in 20% of those using insulin and 12% not using insulin (Klein et al. *Ophthalmology* 1984).

Retinal Vein Occlusion: Another Retinal Vascular Disease and the Third Indication for VEGF Ophthalmic Therapies

Retinal vein occlusion (RVO) is a common cause of vision loss in older populations and can be divided into branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO); the former is the result of an occlusion at the arteriovenous intersection and the latter is an occlusion at or proximal to the lamina cribosa of the optic nerve (where the central retinal vein exits the eye) (Wong and Scott *NEJM* 2010). RVO affects roughly 16 million people worldwide (Rogers et al. *Ophthalmology* 2010). In a population-based cohort study, it was determined that the 10-year incidence of RVO was 1.6% (Cugati et al. *Arch Ophthalmol* 2006). In 10% of patients with RVO in one eye, occlusion develops in the other eye over time. Overall, the strongest risk factors for branch RVO are hypertension, diabetes, dyslipidemia, cigarette smoking, and renal disease, the majority of which are expected to increase in population affected over time (Wong et al. *Ophthalmology* 2005).

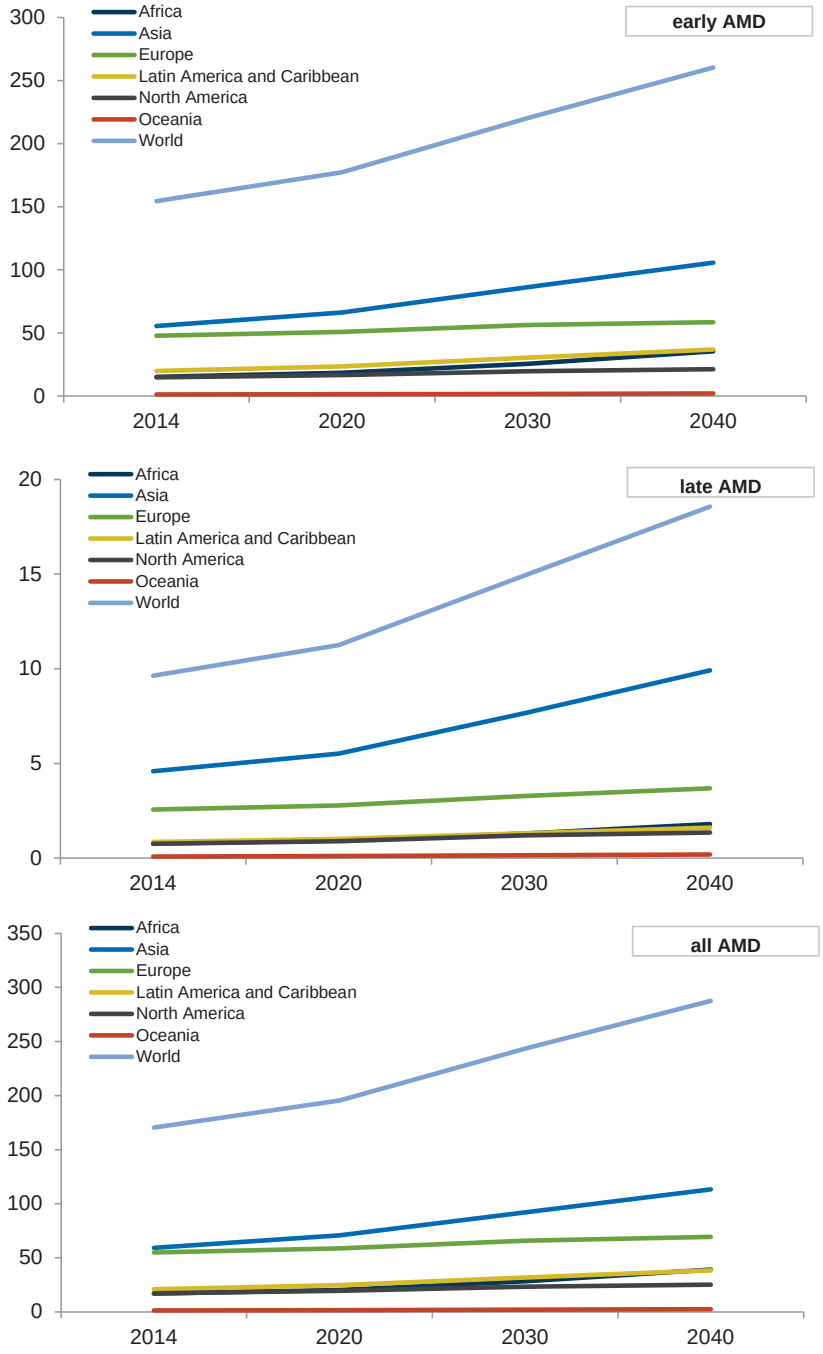
In exhibit 4, we report published estimates of the population with AMD, DME, and RVO in the United States as well as other areas. With the aging population of baby boomers, the population of individuals with eye diseases is expected to increase as well. As shown in exhibit 5, on the following page, the number of people with AMD is projected to grow globally to 196 million in 2020 and 288 million by 2040.

Exhibit 4
Avalanche Biotechnologies, Inc.
Populations With AMD, DME, and RVO

Disease	Region	Estimated Population
AMD	U.S.	15 million
Wet AMD	U.S.	1.7 million
AMD	E.U.	2.5 million
Bilateral AMD	E.U.	1.1 million
DME	U.S.	560,000
RVO	U.S., E.U., Asia, Australia	16.4 million
CRVO	U.S., E.U., Asia, Australia	2.5 million
BRVO	U.S., E.U., Asia, Australia	13.9 million

Sources: Genentech reports, EUREYE study, Rogers et al. *Ophthalmology* 2010, BrightFocus Foundation

Exhibit 5
Avalanche Biotechnologies, Inc.
AMD Projected Growth by Region



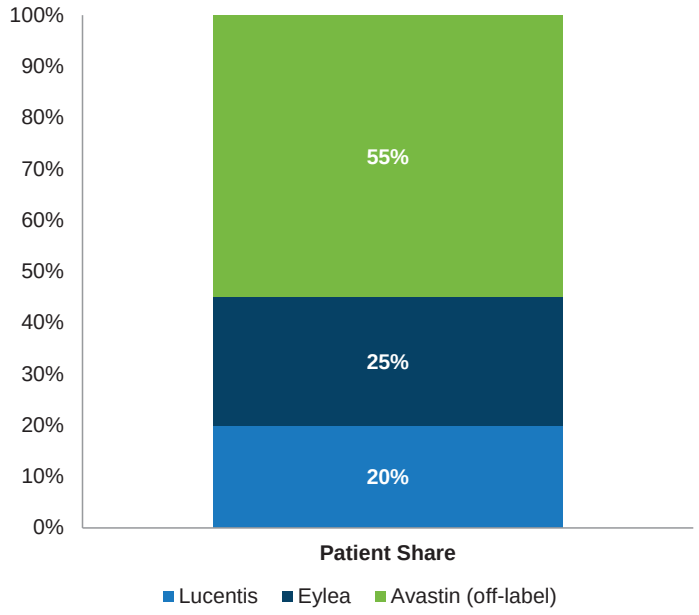
Source: Wong et al. *Lancet Global Health* 2014

Vascular endothelial growth factor (VEGF) is a naturally occurring glycoprotein in the body that can regulate two processes of blood vessel formation: angiogenesis (vessel formation from pre-existing vessels) and vasculogenesis (new vessel formation that occurs through the synthesis of endothelial cells). VEGF has been shown to be sufficient in physiologic blood vessel formation as well as pathologic blood formation, and is therefore one of the most studied targets for new potential drugs against neovascular diseases (Semeraro et al. *Drug Design, Development, and Therapy* 2013).

Current VEGF Therapies

Global sales of brand market products Lucentis and Eylea were over $6 billion in 2013, with about $3.3 billion in the United States and $2.8 billion in territories outside the United States (primarily the European Union, Japan, and Australia). Exhibit 6, below, shows the patient share by volume in the United States for therapies that target the VEGF receptor. Exhibit 7, on the following page, shows the quarterly sales of Eylea and Lucentis since launch in the top panel and the percentage of total brand revenue since launch for both products in the bottom panel. Lucentis, approved in second quarter 2005, recorded $380 million in U.S. sales in its first year and quickly ramped up from there to $815 million in 2006 and $875 million in 2007. Eylea, which launched in fourth quarter 2011, had U.S. sales of $583 million for the first four quarters after launch and $1.4 billion in sales in 2013 as it continued to gain market share against Lucentis. The product is now annualizing sales of more than $1.6 billion, again suggesting the power of reduced dosing frequency in this market.

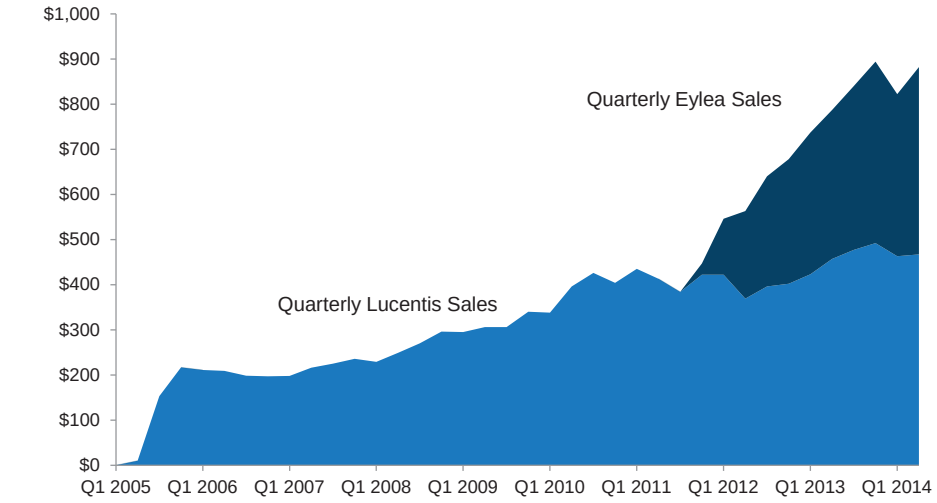
Exhibit 6
Avalanche Biotechnologies, Inc.
Patient Share Volume for Anti-VEGF Therapies

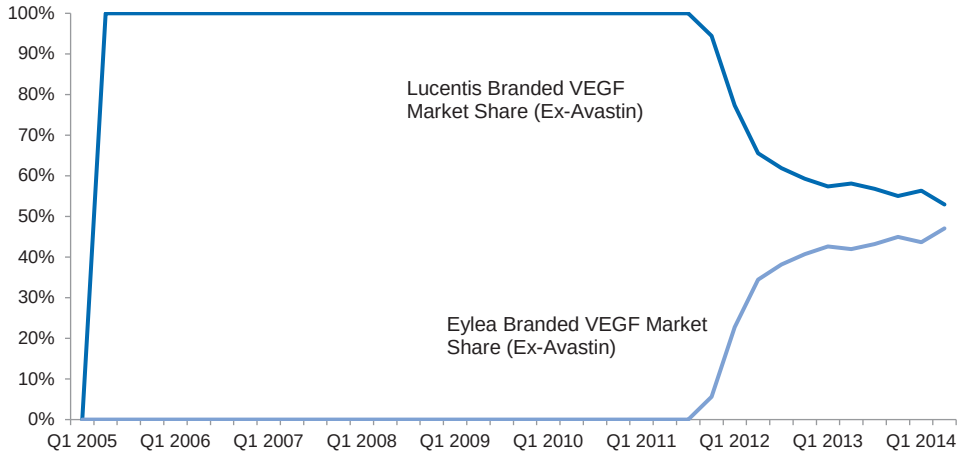


Source: Company reports

Exhibit 7
Avalanche Biotechnologies, Inc.

Total U.S. Branded Revenue and Market Shares for Lucentis (Q2 2005) and Eylea (Q4 2011) Launches



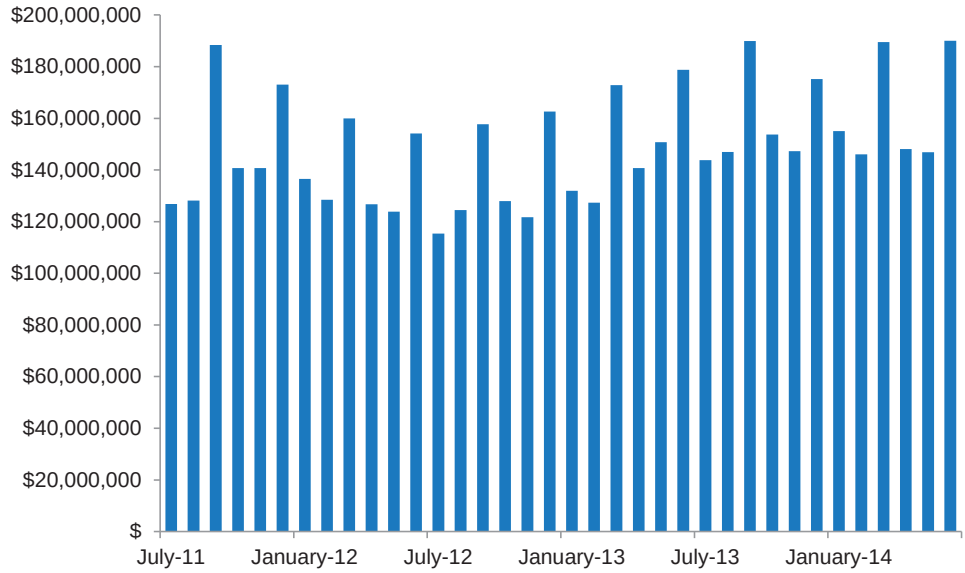


Source: Company reports, William Blair & Company L.L.C.

Lucentis Was the First Brand Product to Market for the Treatment of Wet AMD, DME, and RVO

Lucentis is a recombinant humanized monoclonal antibody (called ranibizumab) intravitreal injection that was approved for wet AMD in June 2006, RVO in June 2010, and DME in August 2012. Lucentis is a VEGF inhibitor that binds to VEGF-A, a protein that has been shown to play a critical role in the growth of new blood vessels and leakiness of existing blood vessels. The drug was initially developed by Genentech, which was subsequently acquired by Roche. According to Roche, sales in the United States were $1.829 billion in 2013, and as shown in exhibit 8, the monthly sales of Lucentis since 2011 as reported by IMS Health have been in the range of $120 million to $190 million, with roughly $1 billion in sales for the first half of 2014.

Exhibit 8
Avalanche Biotechnologies, Inc.
Lucentis Monthly Sales



Year	Sales ($)
2012	$1,639,304,431
2013	$1,859,167,036
1H 2014	$975,630,854

Source: IMS Health

Lucentis has been tested in 27 clinical trials in 10,500 patients over 13 years. Exhibit 9, on the following page, shows the timeline of completed U.S. trials from the first injection in 2000.

Exhibit 9
Avalanche Biotechnologies, Inc.
Lucentis U.S. Trial Timeline

Trial	Indication	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
								wAMD approval				RVO approval		DME approval	
RIDE	DME														
RISE	DME														
CRUISE	RVO														
BRAVO	RVO														
HARBOR	wAMD														
SAILOR	wAMD														
HORIZON EXT	wAMD														
PIER	wAMD														
ANCHOR	wAMD														
MARINA	wAMD														
FOCUS	wAMD														
2508 EXT	wAMD														
STUDY 2425	wAMD														
STUDY 1770	wAMD														
STUDY 2128	wAMD														

Source: Lucentis reports

The initial pivotal Phase III trial, entitled MARINA, was a two-year randomized, multicenter, double-masked, sham-injection-controlled study involving 716 patients with minimally classic lesions or occult with no classic lesions that were randomized to a monthly sham (N=238), monthly Lucentis at 0.3 mg (N=238), and the now FDA-approved dose of monthly Lucentis at 0.5 mg (N=240). The primary endpoint of the study was the proportion of patients losing fewer than 15 letters from baseline visual acuity at 12 months. As shown in exhibit 10, the mean change in visual acuity from baseline over 24 months was a 21.5-letter difference (an increase of 6.6 letters in Lucentis 0.5 mg versus a decline of 14.9 letters in the sham group). The primary endpoint was met, with 90% of patients on Lucentis maintaining vision versus 52.9% on sham after 24 months.

Exhibit 10
Avalanche Biotechnologies, Inc.
Pivotal Phase III Trial (MARINA) Results With Lucentis

Lucentis 0.5 mg	Sham
N=240	N=238
6.6 letters	-14.9 letters

Study was conducted over 24 months

Source: Lucentis reports

The second pivotal Phase III trial, entitled ANCHOR, was a two-year, multicenter, double-masked active-treatment-controlled study involving 423 patients with predominantly classic lesions that were randomized to verteporfin PDT monthly sham injections (N=143), monthly Lucentis 0.3 mg injections (N=140), and monthly Lucentis 0.5 mg injections (N=139). The primary endpoint was the same as the MARINA trial. As shown in exhibit 11, the mean visual acuity from baseline over 24 months in the ANCHOR trial was 20.5 letters (an increase of 10.7 letters with Lucentis versus a decline of 9.8 in verteporfin PDT) and the study also met the primary endpoint, with 89.9% of patients on monthly Lucentis maintaining vision versus 65.7% of patients on verteporfin PDT. The difference in increases in mean visual acuity in ANCHOR versus MARINA might be a result of the patients recruited for the study, with ANCHOR using predominantly classic choroidal neovascularization (CNV) patients where the lesions can be distinctly visualized.

Exhibit 11
Avalanche Biotechnologies, Inc.
Pivotal Phase III Trial (ANCHOR) Results With Lucentis

Lucentis 0.5 mg	Verteporfin PDT
N=139	N=143
10.7 letters	-9.8 letters

Study was conducted over 24 months

Source: Lucentis reports

In addition to the two pivotal Phase III trials, a third Phase III trial was run to assess monthly dosing of Lucentis versus less frequent dosing. In the trial, called HARBOR, a 24-month safety and efficacy trial with treatment-naive patients with classic, minimally classic, or purely occult CNV were randomized to Lucentis 0.5 mg monthly and 0.5 mg less frequent dosing for a 12-month active-treatment-controlled period. The primary endpoint of the study was the mean change in best corrected visual acuity (BCVA) from baseline at month 12. As shown in exhibit 12, on the following page, the mean change in BCVA from baseline was an increase of 10.1 letters in the monthly injection group (11.3 mean injections) versus an increase of 8.2 letters in the less frequent injection group (7.7 mean injections).

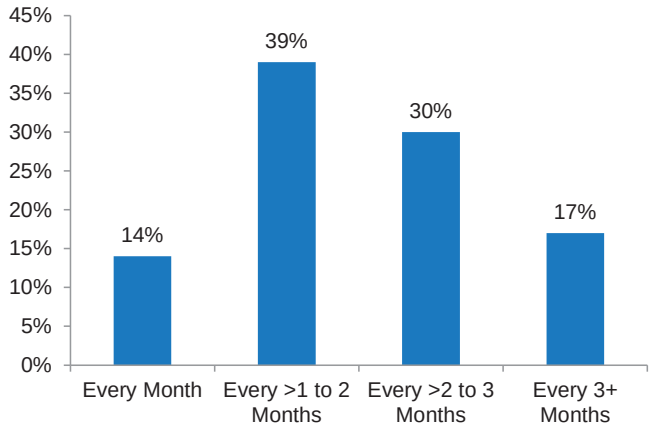
Exhibit 12
Avalanche Biotechnologies, Inc.
HARBOR Results at 12 Months

Lucentis 0.5 mg monthly	Lucentis 0.5 mg less frequent
N=275	N=275
10.1 letters	8.2 letters
11.3 mean injections	7.7 mean injections

Source: Lucentis reports

The average treatment interval following the three initial monthly doses in the HARBOR study was 8.7 weeks in the less frequent arm compared with the monthly dosing arm in year one. As shown in exhibit 13, roughly 39% of patients were dosed at a frequency of more than one to two months, with 30% more than two to three months, and 17% of patients every three or more months.

Exhibit 13
Avalanche Biotechnologies, Inc.
HARBOR Injection Rates in Less Frequent Injection Group



Source: Lucentis label

The HARBOR study did not reach a statistically significant result for the study's primary endpoint (P=0.8145), which was composed of three comparisons: a superiority comparison (2 mg monthly versus 0.5 mg monthly) and two non-inferiority comparisons (2 mg as needed and 0.5 mg as needed versus 0.5 mg monthly [Busbee et al. *Ophthalmology* 2013]). The label for Lucentis for wet AMD continues to recommend Lucentis administration by intravitreal injection once a month, and although it is not as effective, patients may be treated with three monthly doses followed by less frequent dosing with regular assessment.

The second indication received for Lucentis was for RVO, where two pivotal Phase III trials were conducted. BRAVO, one of the pivotal Phase III studies, was conducted at 93 sites with a six-month sham-injection-controlled study and an additional six months of follow-up in 397 patients with macular edema following branch retinal vein occlusion (BRVO). CRUISE was a pivotal Phase III study conducted at 95 sites with a six-month sham-injection control with an additional six months of follow-up in 392 patients who had macular edema following central retinal vein occlusion (CRVO).

In BRAVO, patients with BRVO were randomized to three groups: sham injection (N=130), Lucentis 0.3 mg (N=135), or Lucentis 0.5 mg (N=130). The primary endpoint was mean change from baseline in BCVA at month six. As shown in exhibit 14, the mean change in baseline increased to 11.6 letters at one month, 15.3 at three months, and 18.3 at the primary endpoint of six months versus an increase of 3.1 letters at one month, 4.5 at three months, and 7.3 at six months in the sham group. In addition, 54.5% of sham-treated patients received rescue grid laser treatment within the first six months compared with 19.8% in the Lucentis group.

Exhibit 14
Avalanche Biotechnologies, Inc.
BRAVO Trial Primary Endpoint With Lucentis for BRVO

Time	Lucentis 0.5 mg (N=130)	Sham (N=130)
Day 7	11.6 letters	3.1 letters
3 months	15.3 letters	4.5 letters
6 months	18.3 letters	7.3 letters

Source: Lucentis reports

For the CRUISE study, 392 patients were randomized to sham (N=130), Lucentis 0.3 mg (N=132), and Lucentis 0.5 mg (N=130), and were treated for six months with the primary endpoint similar to the BRAVO study. Exhibit 15 shows the results of the CRUISE study, including statistically significant differences throughout the six-month period between the Lucentis 0.5 mg group and sham. At the six-month period, the Lucentis and sham-treated groups showed a mean change of a 14.9 increase in letters and a 0.8 increase in letters, respectively. The label for Lucentis suggests a monthly therapy of 0.5 mg to be administered by intravitreal injection once a month for both forms of RVO.

Exhibit 15
Avalanche Biotechnologies, Inc.
CRUISE Trial Primary Endpoint With Lucentis for CRVO

Time	Lucentis 0.5 mg (N=130)	Sham (N=130)
Day 7	9.9 letters	0.5 letters
3 months	12.2 letters	0.2 letters
6 months	14.9 letters	0.8 letters

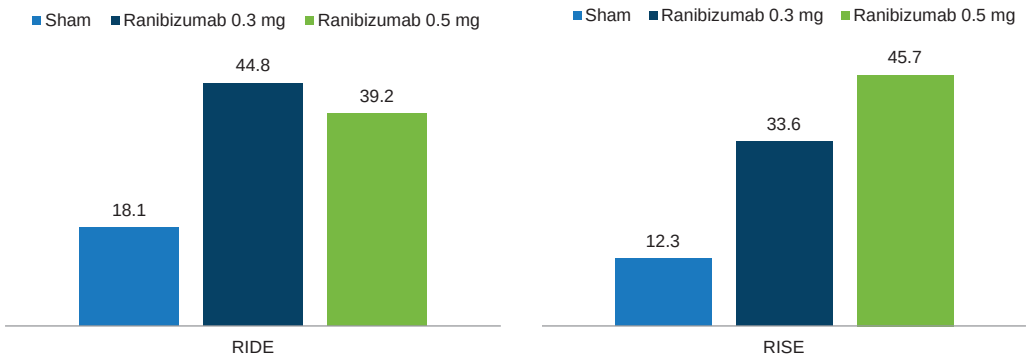
Source: Lucentis reports

For the treatment of DME, the latest approval received by Lucentis, two clinical trials were conducted to assess the impact of Lucentis, RIDE and RISE. The studies recruited 759 patients with DME in two identical multicenter, double-masked, sham injection-controlled studies that were randomized to three groups (with one eye per subject) of sham injection (N=247), Lucentis 0.3 mg (N=250), and Lucentis 0.5 mg (N=252) for monthly dosing over a 24-month period. Beginning at month three, all patients were evaluated monthly for the need for macular laser. The primary efficacy measure for the study was the proportion of patients gaining greater than or equal to 15 letters in the BCVA score from baseline at 24 months (which corresponds to three lines on an eye chart).

Exhibit 16, on the following page, shows the primary efficacy endpoints of both the RISE and RIDE studies. In RISE, the 0.3 mg Lucentis group had 44.8% of patients with a gain of greater than or equal to 15 letters versus 39.2% in the 0.5 mg Lucentis group and 18.1% in the sham group. In RIDE, the 0.3 mg Lucentis group had efficacy of 33.6% compared with 0.5 mg Lucentis at 45.7% and the sham group at 12.3%. As shown in exhibit 17, on the following page, the mean change in visual acuity was an increase of 12.5 letters in the 0.3 mg Lucentis group, 11.9 in the 0.5 mg Lucentis group, and 2.6 in the sham group in the RISE study and an increase of 10.9 letters in the 0.3 mg Lucentis group, 12.0 in

the Lucentis 0.5 mg group, and 2.3 in the sham group for the RIDE study. Lastly, 37.6% of the 0.3 mg Lucentis group received macular laser therapy, with 0.7 mean treatments; in the sham group, 72% of patients received macular laser therapy, with 1.7 mean treatments. Based on these results, the label indication in Lucentis for DME is for 0.3 mg administered by intravitreal injection once a month.

Exhibit 16
Avalanche Biotechnologies, Inc.
RIDE and RISE Primary Efficacy Endpoint



Source: Nguyen et al. *Opthalmology* 2012

Exhibit 17
Avalanche Biotechnologies, Inc.
Mean Change in Visual Acuity in RIDE and RISE Trials for DME

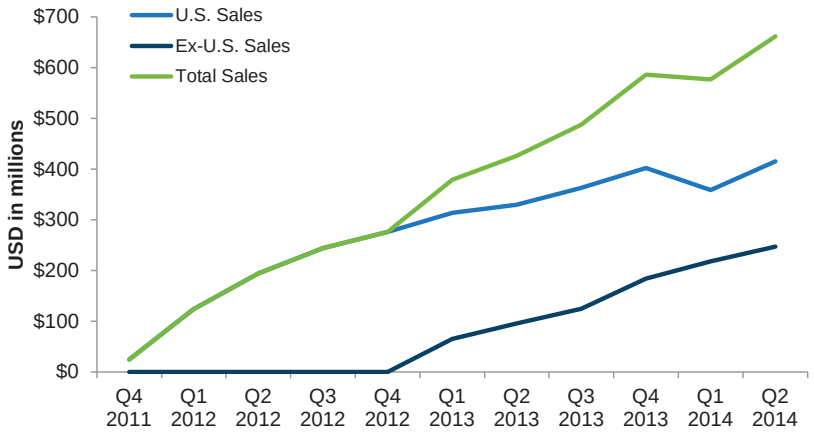
Trial	Sham	Ranibizumab 0.3 mg	Ranibizumab 0.5 mg
RISE	2.6 letters	12.5 letters	11.9 letters
RIDE	2.3 letters	10.9 letters	12.0 letters

Source: Nguyen et al. *Opthalmology* 2012

From a clinical data standpoint, Lucentis paved the way in showing VEGF inhibition, leading to impressive patient outcomes in wet AMD, DME, and RVO. However, Genentech/Roche was unable to show that a decreased rate of monthly injections was able to sustain the benefit. The difficulties in keeping patients compliant with monthly intravitreal injections left the Lucentis franchise vulnerable to another VEGF-targeting therapy, Eylea, which was developed by Regeneron and entered the market in 2011 with a reduced dosing frequency.

Eylea by Regeneron Has Gained Significant Market Share From Lucentis Since Launch in 2011
Eylea is a soluble decoy receptor fusion protein that is purified and formulated for intraocular injection. The binding affinity of intravitreal aflibercept to VEGF is substantially greater than Lucentis, which was initially hypothesized to be the reason for reduced injections compared with Lucentis (Holash et al. *PNAS* 2002). In exhibit 18, we break down Eylea sales into sales within the United States and outside the United States, illustrating the impressive ramp up in both markets for Eylea over the past several quarters.

Exhibit 18
Avalanche Biotechnologies, Inc.
Eylea Revenue Since Launch (November 21, 2011)



		Q4 2011 (11/21/11-12/31/11)	Q1 2012	Q2 2012	Q3 2012	Q4 2012	Q1 2013	Q2 2013	Q3 2013	Q4 2013	Q1 2014	Q2 2014
($ in millions)												
U.S. Sales		$25	$124	$194	$244	$276	$314	$330	$363	$402	$359	$415
Ex-U.S. Sales		NA	NA	NA	NA	NA	$65	$96	$125	$184	$218	$247
Total Sales		**$25**	**$124**	**$194**	**$244**	**$276**	**$379**	**$426**	**$488**	**$586**	**$577**	**$662**
Growth Rates												
U.S.	**Growth Q/Q**	NA	397.99%	56.45%	25.77%	13.11%	13.77%	5.10%	10.00%	10.74%	-10.70%	15.60%
	Growth Y/Y	NA	NA	NA	NA	NA	153.23%	70.10%	48.77%	45.65%	14.33%	25.76%
Ex-U.S.	**Growth Q/Q**	NA	NA	NA	NA	NA	NA	47.69%	30.21%	47.20%	18.48%	13.30%
	Growth Y/Y	NA	NA	NA	NA	NA	NA	NA	NA	NA	235.38%	157.29%
Total	**Growth Q/Q**	NA	397.99%	56.45%	25.77%	13.11%	37.32%	12.40%	14.55%	20.08%	-1.54%	14.73%
	Growth Y/Y	NA	NA	NA	NA	NA	205.65%	119.59%	100.00%	112.32%	52.24%	55.40%

Source: Regeneron reports

The Phase III pivotal studies for Eylea in wet AMD, called VIEW 1 and VIEW 2, were similarly designed prospective double-masked, parallel-group active-controlled, randomized designs. VIEW 1 enrolled 1,210 patients and VIEW 2 enrolled 1,202 patients, randomizing them into four different treatment groups and monitoring them for 52 weeks (exhibit 19).

Exhibit 19
Avalanche Biotechnologies, Inc.
VIEW 1 and VIEW 2 Dosing Schedule

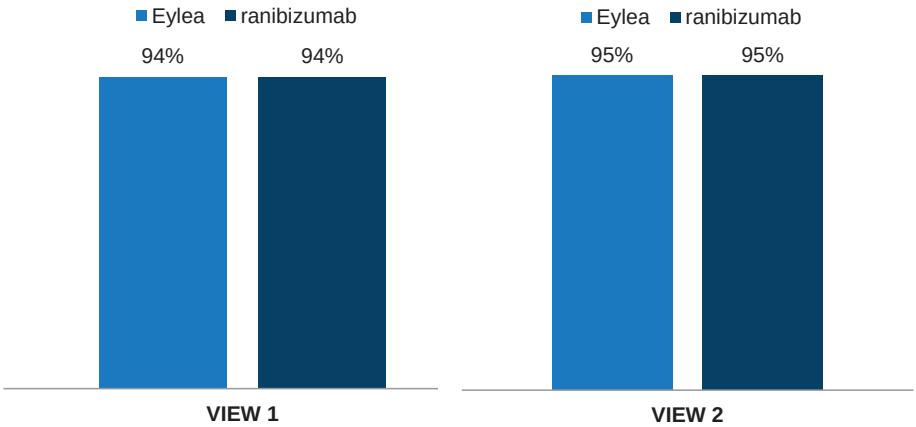
		Weeks													
Treatment	Regimen	0	4	8	12	16	20	24	28	32	36	40	44	48	52
Eylea	2 mg every 8 weeks	X	X	X		X		X		X		X		X	
Eylea	2 mg every 4 weeks	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Eylea	0.5 mg every 4 weeks	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Ranibizumab	0.5 mg every 4 weeks	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Source: Regeneron reports

The primary endpoint of the study was the maintenance of vision (fewer than 15 letters lost) based on BCVA at 52 weeks with Eylea versus Lucentis. As shown in exhibit 20, in VIEW 1, Eylea dosed every two months (after an initial three monthly doses) resulted in 94% maintenance of vision compared with ranibizumab's 94% with monthly doses. VIEW 2 showed similar results, with Eylea dosed every two months (after an initial three monthly doses) resulting in 95% of patients maintaining vision and Lucentis with monthly doses resulting in 95%. This resulted in a label indication for Eylea in wet AMD for a recommended dose of 2 mg administered by intravitreal injection every month for the first three months, followed by 2 mg once every two months.

Exhibit 20
Avalanche Biotechnologies, Inc.

VIEW 1 and VIEW 2 Primary Endpoint: Maintenance of Vision at 52 Weeks Versus Baseline

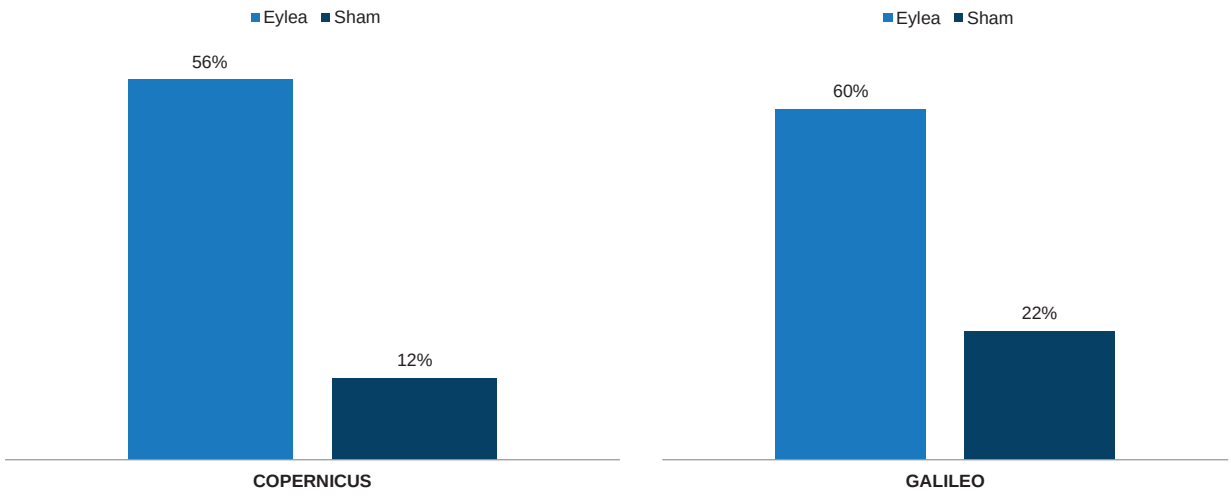


	Ranibizumab 0.5 mg every 4 weeks	Eylea 2 mg every 4 weeks	Eylea 0.5 mg every 4 weeks	Eylea 2 mg every 8 weeks
Change in ETDRS BCVA (mean letters ± SD)	9.4 ±13.5	7.6 ± 12.6	9.7 ± 14.1	8.9 ± 14.4

Source: Regeneron reports

Eylea is also indicated for the treatment of macular edema following CRVO with two Phase III clinical trials, COPERNICUS and GALILEO, providing supporting information. Both studies were designed with treatment-naive patients randomized 3:2 to Eylea at 2 mg administered every four weeks for six months and sham control. The primary endpoint of the study, similar to the Lucentis trials, was the proportion of patients who gained at least 15 letters in the BCVA from baseline to 24 weeks. As shown in exhibit 21, Eylea demonstrated significant effects in both studies, with 56% of patients gaining at least 15 letters in COPERNICUS and 60% of patients in GALILEO.

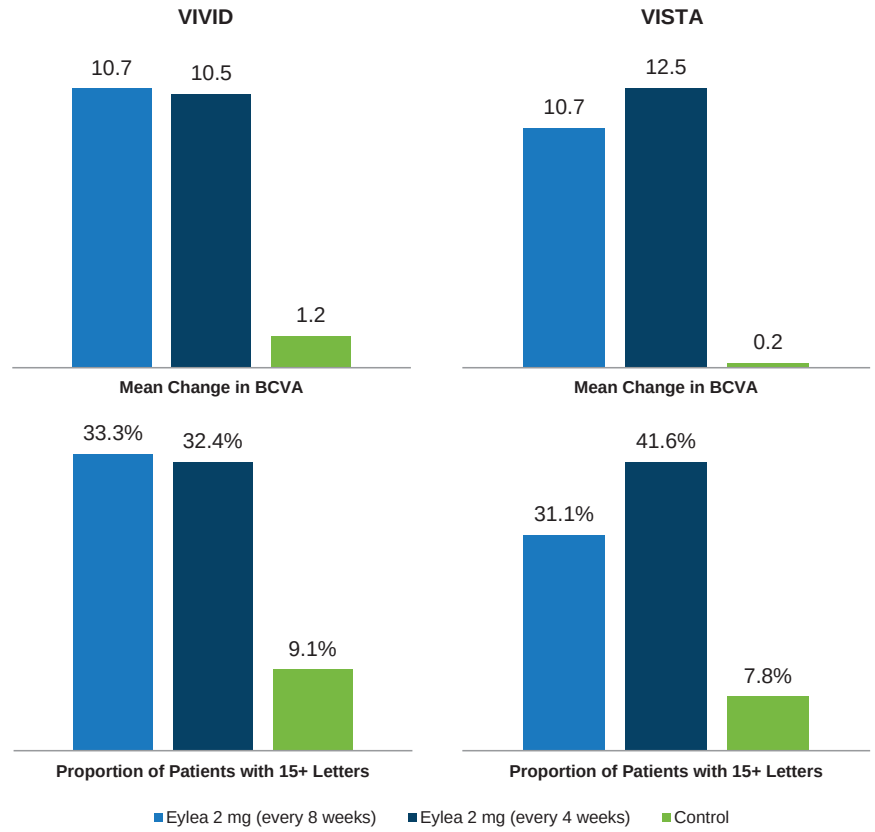
Exhibit 21
Avalanche Biotechnologies, Inc.
COPERNICUS and GALILEO Phase III Results With Eylea for CRVO



Source: Regeneron reports

The most recent approval for Eylea was in DME. The safety and efficacy was tested in two clinical trials, VIVID and VISTA, for a total of 862 patients. Patients were randomly assigned to three dosing regimens: Eylea 2 mg administered every eight weeks following five initial monthly injections (N=135 in VIVID and N=151 in VISTA), Eylea 2 mg administered every four weeks (N=136 in VIVID and N=154 in VISTA), and macular laser photocoagulation (at baseline and as needed, N=132 in VIVID and N=154 in VISTA). Exhibit 22, on the following page, shows the results from VIVID and VISTA, with mean changes of a 10.7 increase in BCVA in the eight-week group and a 10.5 increase in the four-week group compared with a 1.2 increase in the control treatment in VIVID, and mean changes of a 10.7 increase in the eight-week group, a 12.5 increase in the four-week group, and a 0.2 increase in the control group in VISTA. Further, the proportion of patients who gained at least 15 letters from baseline were 33.3% in the eight-week group, 32.4% in the four-week group, and 9.1% in the control in VIVID and 31.1% in the eight-week group, 41.6% in the four-week group, and 7.8% in the control in VISTA.

Exhibit 22
Avalanche Biotechnologies, Inc.
VIVID and VISTA Results for Eylea in DME

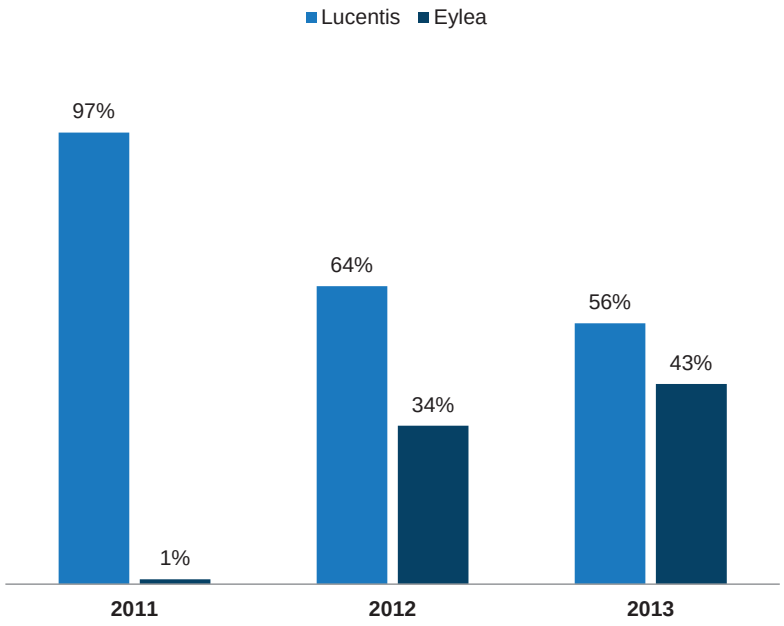


Source: Regeneron reports

As a result of the introduction of Eylea into the retinal disease space in 2011, the market share for Lucentis eroded significantly, as shown in exhibit 23. We believe that Avalanche's AVA-101 therapy would provide a significant advantage over both Eylea and Lucentis based on the functional cure that it could provide to patients by eliminating the need for recurrent injections. And given the significant market share gains made by reducing the frequency of dosing from once a month to once every other month (aside from loading doses), it is not unreasonable to believe the approval of a curative therapy would be able to carve out significant market share pending an approval.

However, aside from Lucentis and Eylea, there is a much lower-cost agent already available for use, off-label Avastin, Roche's VEGF inhibitor for oncology, which is prepared for intravitreal injections through compounding pharmacies.

Exhibit 23
Avalanche Biotechnologies, Inc.
Lucentis and Eylea Brand Market Share Since 2011 (Eylea Launch)

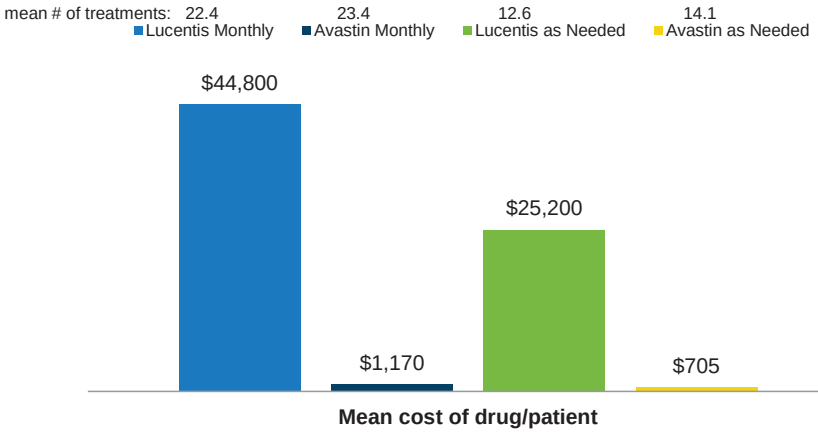


Source: Allergan reports

Brand Market Affected by Off-Label Avastin Use in Over Half of AMD Cases

In its 2012 *Preferences and Trends Survey* report, the American Society of Retina Specialists reported that 66.5% of retina specialists said they used bevacizumab (Avastin) monotherapy to treat typical wet AMD with subfoveal CNV of up to one disc diameter in size, and we still believe it is one of the most commonly used drug in the United States to treat wet AMD (Major and Hariprasad, *Ophthalmic Surg Lasers Imaging Retina* 2013). Avastin, a drug also marketed by Roche, is prescribed off-label for wet because Avastin has target specificity similar to Lucentis and Avastin is available at a low cost, as shown in exhibit 24 (Rosenfeld et al. *NEJM* 2006 and Avery et al. *Ophthalmology* 2006).

Exhibit 24
Avalanche Biotechnologies, Inc.
Mean Cost of Drug/Patient in CATT After Two Years

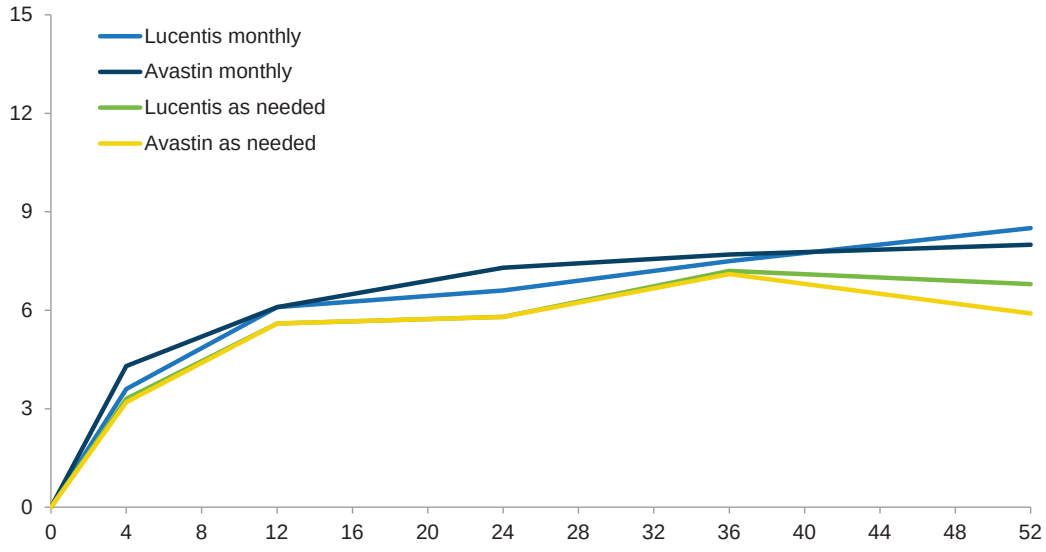


Source: Martin et al. *Ophthalmology* 2012

The Comparisons of Age-Related Macular Degeneration Treatment Trials (CATT) was initiated to assess the efficacy and safety of Lucentis (ranibizumab) and Avastin (bevacizumab) to determine if the as-needed regimen being prescribed with Avastin would compromise long-term vision compared with the monthly regimen that is on-label for Lucentis. The study enrolled 1,208 patients and randomly assigned them to four groups according to drug and administration method after the first mandatory intravitreal injection: Lucentis monthly (N=301), Avastin monthly (N=286), Lucentis as needed (N=298), and Avastin as needed (N=300). The 0.5 mg dose for Lucentis (the FDA-approved dosage for wet AMD) and 1.25 mg of Avastin were both administered in 0.05 ml of solution. The primary outcome of the study was the mean change in visual acuity between baseline and one year with secondary outcomes, including the proportion of patients who did not experience a change in visual acuity of 15 letters or more and number of injections.

As shown in exhibit 25, visual acuity was improved in all four study groups with most of the improvement taking place within the first six months. Lucentis given as needed was not statistically different from Avastin given monthly. The proportion of patients with visual acuity benefits was not different between the groups: 94.4% in the Lucentis monthly group, 94% in the bevacizumab monthly group, 95.4% in the Lucentis as-needed group, and 91.5% in the Avastin as-needed group (P=0.29). The study concluded at the one-year time point that a head-to-head comparison of Avastin and Lucentis had equivalent effects on visual acuity at all points in time. In addition, the study showed that good results could be achieved with fewer-than-monthly injections for both drugs.

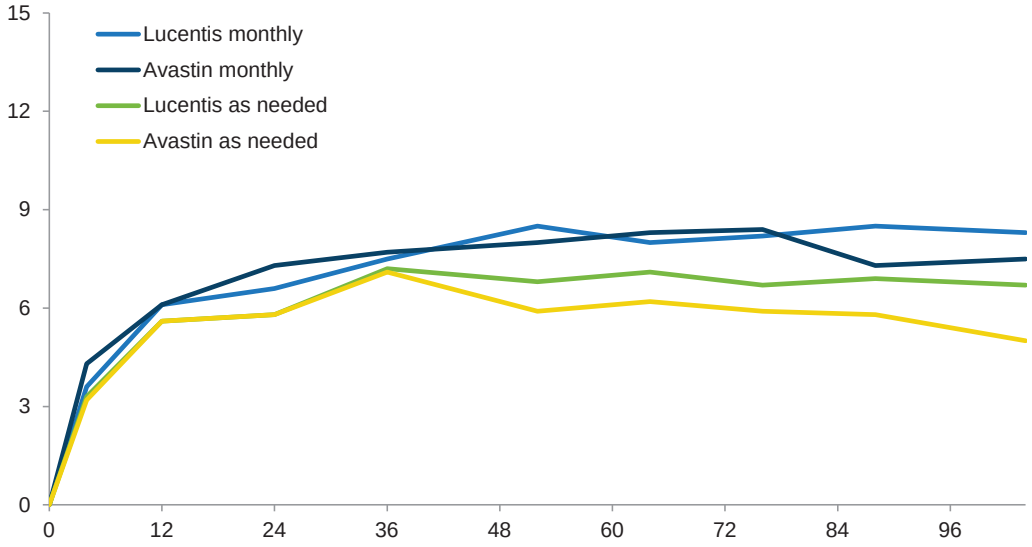
Exhibit 25
Avalanche Biotechnologies, Inc.
Primary Endpoint After One Year in CATT Comparison of Lucentis and Avastin



Source: CATT Research Group *NEJM* 2011

The analysis of the two-year results of CATT shows that the mean gain in visual acuity was similar for both drugs over the two-year period, with the treatment-as-needed group resulting in a smaller gain (exhibit 26, Martin et al. *Ophthalmology* 2012). In addition, some safety effects were seen at the one-year point that were assessed and not found at the second-year time point in the study.

Exhibit 26
Avalanche Biotechnologies, Inc.
CATT Patients Treated With Same Dosing Regimen for Two Years



Source: Martin et al. *Ophthalmology* 2012

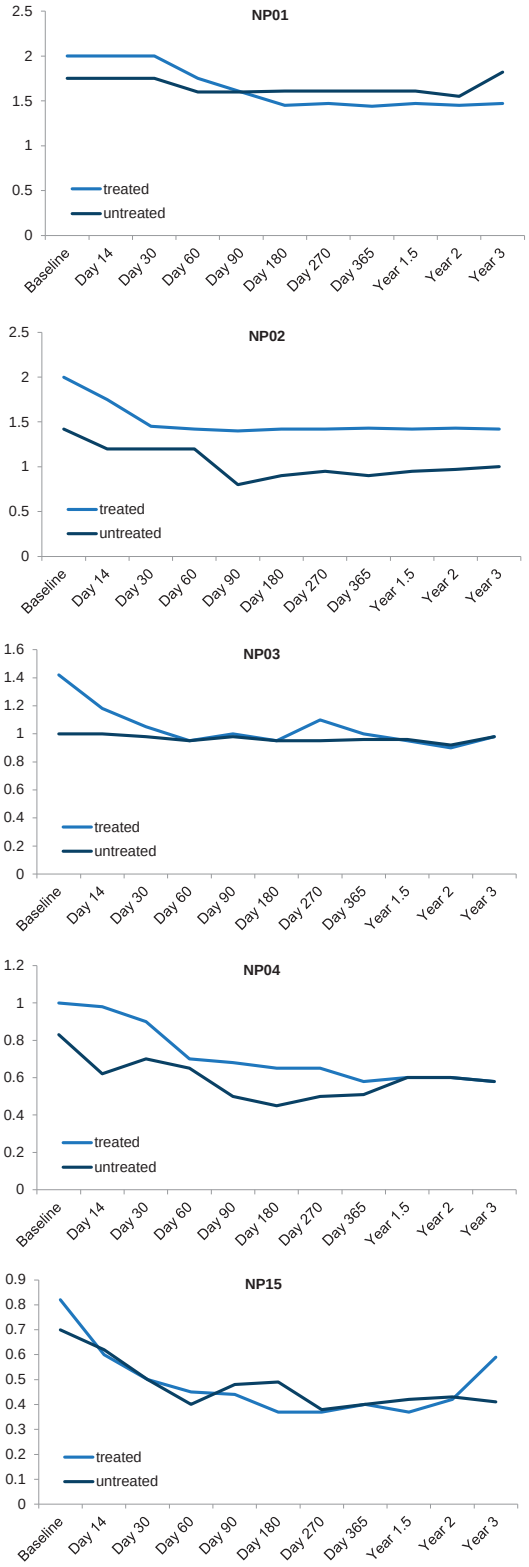
Gene Therapy Has Already Had Success in Ocular Diseases

Treatment of Leber Congenital Amaurosis Type 2 With Adeno-Associated Virus (AAV) Single Injection Provides Proof of Concept

In a study published by Testa et al. in *Ophthalmology* in 2012, the authors detailed a three-year follow-up after unilateral subretinal delivery of an AAV in patients with Leber congenital amaurosis type 2 (LCA2). In this study, five patients with LCA2 and RPE65 gene mutations were given a single subretinal injection of AAV2-hRPE65v2 and evaluated before surgery and at designated follow-ups at 1, 2, 3, 14, 30, 60, 90, 180, 270, and 365 days, as well as 1.5 and 3.0 years. As shown in exhibit 27, on the following page, the results showed a statistically significant improvement of visual acuity between baseline and three years after treatment in the treated eye ($P<0.001$) as well as the untreated eye ($P=0.041$). The maximum visual acuity gains were seen at 6 months after treatment in three subjects and 18 months in one subject. In addition, there was an enlargement of the visual field (average values 1,058 degrees^2 versus 4,630 degrees^2 three years after treatment) and a statistically significant difference in pupillary constriction of the treated eye compared with the untreated eye in three patients at one- and three-year points ($P<0.05$). Lastly, no patients experienced serious adverse events related to the vector in the three-year follow-up period.

Although the results show some waning efficacy by the end of the three-year follow-up period, more importantly, this study shows proof of concept in the ability of an AAV delivery to treat ocular diseases with a single intraretinal injection with no vector-specific adverse events. We believe this study further validates the potential for gene therapies such as AVA-101 in ophthalmic diseases. And as noted above, the LCA2 gene therapy was administered through an intraretinal injection, similar to the administration of AVA-101.

Exhibit 27
Avalanche Biotechnologies, Inc.
AAV2-hRPE65v2 Results in LCA2



Source: Testa et al. *Ophthalmology* 2013

Comparison of Clinical Trial Efficacy and Dosing Regimen Data Shows Potential for AVA-101 in Wet AMD Patient Population

Exhibit 28, on the following page, compares the clinical trial efficacy (in the most recent clinical trial), as measured by visual acuity improvement, of all therapies in development or currently marketed for wet AMD along with time of measurement, sample size, dosing regimen, and mean number of injections. While obviously tested in only a small number of patients, we believe Avalanche's AVA-101 therapy provides a significant clinical benefit by reducing the number of injections required (for at least 52 weeks) by more than 90% from the existing therapies used to treat the disease while maintaining visual acuity scores on par with the other treatments.

Exhibit 28
Avalanche Biotechnologies, Inc.
Comparison of Visual Acuity Changes and Dosing Differences in Wet AMD Products in Most Recent Clinical Trials

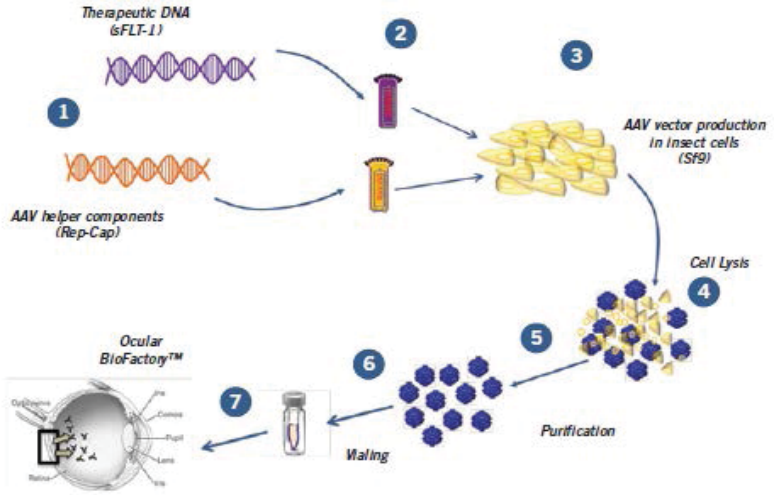
Product	Avastin		Eylea		Lucentis		Fovista	DARPin				AVA-101	
Company	Roche		Regeneron		Roche		Ophthotech	Allergan				Avalanche	
N for Trial(s)	1208 (CATT)		2457 (VIEW)		1323 (AMD)		449 (Phase 2b)	64 (Stage 3, Phase 2)				8 (Phase 1b)	
Time Point	24 weeks	52 weeks	52 weeks	96 weeks	52 weeks	104 weeks	24 weeks	16 weeks		20 weeks		52 weeks	
Dose	1.25 mg	1.25 mg	2 mg	2 mg	0.5 mg	0.5 mg	1.5 mg + 0.5 mg Lucentis	1 mg	2 mg	1 mg	2 mg	10^{10} vector genomes	10^{11} vector genomes
Dosing Regimen	Monthly and As needed	Monthly and As needed	2 mg administered by injection in the eye every 2 months (8 weeks) following 3 initial monthly (4 weeks) injections.		Monthy injections		Monthly doses of Fovista+Lucentis	Patients received doses at start of trial, 4 weeks, and 8 weeks, received sham injections at 12 weeks and 16 weeks				Week 0, Week 4: Lucentis injections, Day 7: AVA-101 (1 injection only)	
Mean No. of Injections in Study	Monthly (52 weeks): 11.9 As needed (52 weeks): 7.7		7	11.2	12	24	6	3				0.33	
Visual Acuity Improvement (No. of Letters on BCVA Scale)	Monthly: +7.3 As needed: +5.8	Monthly: +8.0 As needed: +5.9	+8.4	+7.6	+6.3 (AMD-1*) +11.0 (AMD-2*)	+5.5 (AMD-1*) +10.9 (AMD-2*)	+10.6	+6.3	+8.2	+7.1	+9.0	+8.7	+6.3

*AMD-1 enrolled patients with minimally classic or occult (without classic) CNV lesions, whereas AMD-2 enrolled predominantly classic CNV lesions
Sources: Company reports and William Blair & Company, L.L.C.

Pipeline Aimed at Curative Therapies for AMD and Other Eye Diseases

Avalanche's product pipeline is based on its proprietary Ocular BioFactory platform, which is designed to use an adeno-associated virus (AAV) as a vector to deliver and express a functional gene to cells in the eye to promote continuous protein production (exhibit 29). In general, the AAV platform is nonpathogenic and nonreplicative on its own; the gene-transfer vectors derived from AAVs are non-inflammatory and non-integrative, and they promote long-term expression of the gene of interest. To make an AAV, a DNA strand encoding the target gene, a *cap* gene (that encodes the proteins VP1, VP2, and VP3, which are capsids classified by serotype), and a *rep* gene and helper (which enables replication during the manufacturing process only) are introduced into producer cells.

Exhibit 29
Avalanche Biotechnologies, Inc.
Ocular BioFactory

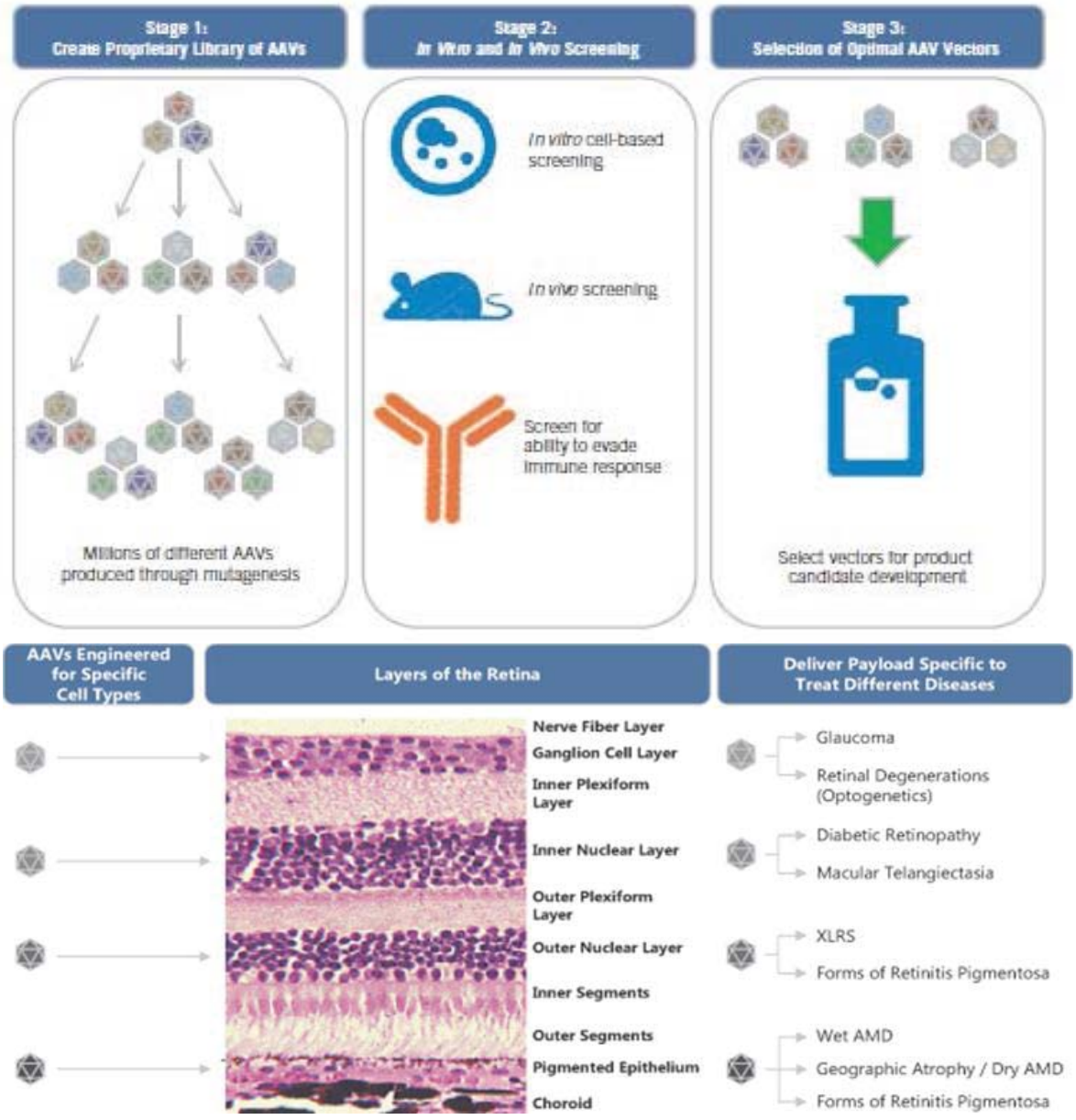


Source: Company reports

The Ocular BioFactory platform features two key proprietary components: a vector screening and optimization system referred to as directed evolution and an industrial manufacturing process based on a "highly efficient and scalable" baculovirus expression system (top panel of exhibit 30, on the following page).

As shown in the bottom panel of exhibit 30, directed evolution allows for the development of individual vectors that are optimized to target different layers of the retina. According to the company's website, production yields are up to 100 times greater than conventional AAV production systems (roughly 3×10^{14} vg/run in conventional transfection production versus more than 10^{16} vg/run with Avalanche's production method).

Exhibit 30
Avalanche Biotechnologies, Inc.
AAV Platform Targeted to Different Layers of the Retina in Directed Evolution



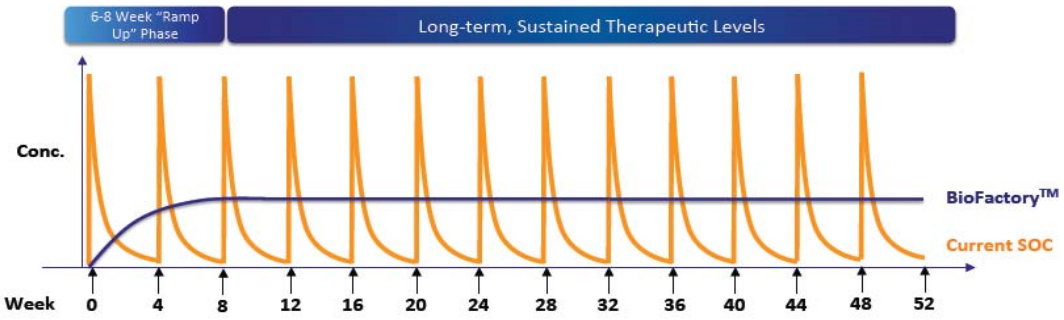
Source: Company reports

AVA-101

AVA-101, the company's lead product, is being developed as a single subretinal injection that is intended to provide a safe and effective treatment for wet AMD without the need for recurring injections that classify the current market leaders in therapy. AVA-101 is made up of the AAV2 vector, which contains a gene encoding sFlt-1, a naturally occurring anti-VEGF protein. VEGF is a homodimeric hormone that induces the proliferation of endothelial cells. One difference between AVA-101 and other therapies is that AVA-101 is administered with an intraretinal injection rather than an intravitreal injection. However, we believe the majority of vitreoretinal surgeons can perform this procedure.

From preclinical studies, AVA-101 reached a therapeutically beneficial level within six to eight weeks of administration. Animal models have shown that AVA-101 can be expressed up to 17 months with no vector-specific adverse events. In addition, preclinical studies did not identify any systemic immune response as a result of the subretinal injections. As shown in exhibit 31, the rationale for AVA-101 is the sustained steady-state delivery of the Ocular BioFactory platform compared with the short-acting current standard of care (SOC).

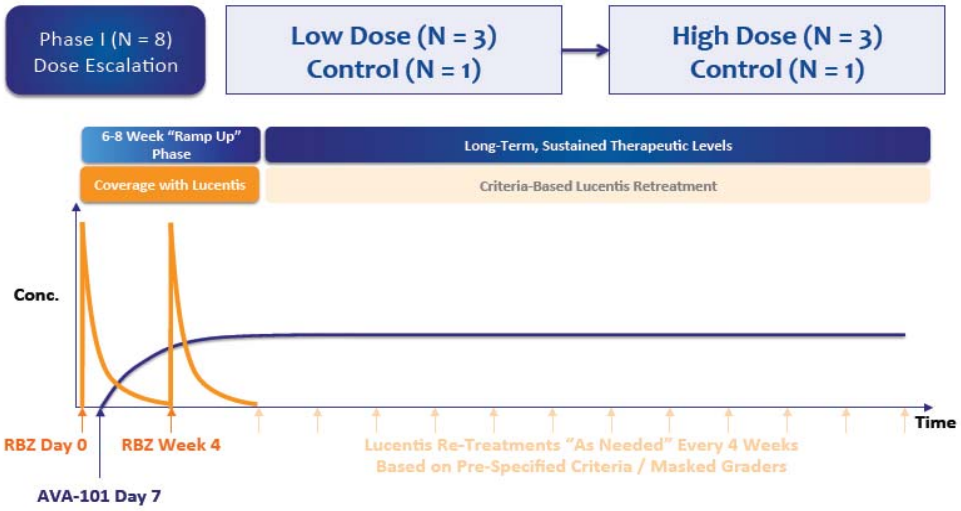
Exhibit 31
Avalanche Biotechnologies, Inc.
Sustained Delivery Pharmacokinestics With BioFactory Compared With Standard-of-Care



Source: Company reports

To date, the company has completed a Phase I trial involving eight subjects that were assessed at 12 months. Endpoints were safety and efficacy measured by improvement in visual acuity, reduction in retinal thickness, and a reduced number of Lucentis rescue injections. As shown in exhibit 32, on the following page, patients were segregated into a control, low AVA-101 dose (10^{10} vector genomes), and high AVA-101 dose (10^{11} vector genomes). All subjects received two initial doses of Lucentis (day zero and four weeks) and the subjects in the active arms received AVA-101 on day seven of the trial.

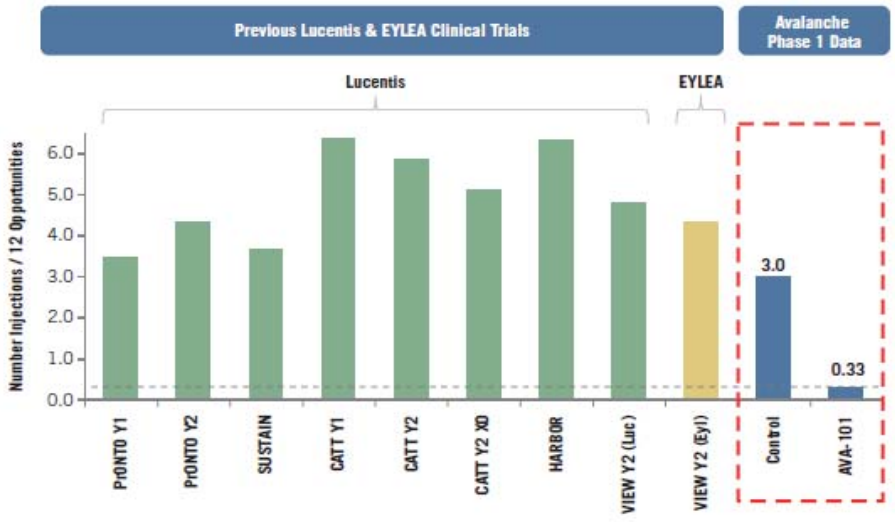
Exhibit 32
Avalanche Biotechnologies, Inc.
AVA-101 Phase I Trial Design



Source: Company reports

At the 12-month point, no significant drug-related safety concerns were observed, with only mild and transient inflammatory responses related to the injection. In addition, there were no clinically significant adverse events and anti-VEGF off-target effects. Based on the data from several of the studies with Lucentis and Eylea (which we presented efficacy data from earlier in this report), when patients are treated only as needed, they receive injections during 29% to 52% of visits, or 3.5 to 6.4 injections out of 12 opportunities. As shown in exhibit 33, subjects receiving high- or low-dose AVA-101 needed an average of only 0.33 rescue treatments over the same period. Furthermore, four out of the six subjects in the AVA-101 treatment arms required no rescue injections and the other two subjects required only one rescue injection each.

Exhibit 33
Avalanche Biotechnologies, Inc.
Number of Injections Per 12 Opportunities Treated With Lucentis, Eylea, and AVA-101



Source: Avalanche S-1

The primary efficacy endpoint of the Phase I trial showed impressive results; AVA-101–treated groups increased visual acuity by an average of 8.7 and 6.3 letters from baseline in the high and low groups, respectively (exhibit 34). In addition, five of the six subjects improved greater than or equal to 5 letters from baseline and three of the six subjects improved greater than or equal to 10 letters from baseline. Although one subject lost six letters from baseline, the company noted that the individual had significant subfoveal scarring at baseline and that those types of individuals would be excluded from future clinical trials. We believe that the results of the initial Phase I trial show the efficacy of AVA-101 and while the study had its limitations, particularly as it was performed in a very small number of patients, we believe the vision benefits were impressive given the significant decrease in the number of injections.

Exhibit 34
Avalanche Biotechnologies, Inc.
Change in Visual Acuity in Phase I Trial With AVA-101

Group	Subject	Baseline Visual Acuity	Week 52 Visual Acuity	Change From Baseline	Average Change From Baseline
Low Dose	R1001	33	40	+7	+8.7
	R1002	28	41	+13	
	R1004	46	52	+6	
High Dose	R2005	56	50	-6	+6.3
	R2006	54	64	+10	
	R2008	34	49	+15	
Control	R1003	28	21	-7	-3.5
	R2007	39	39	+0	

Source: Company reports

Avalanche has initiated a Phase IIa study enrolling 32 subjects that began in August 2012. The trial design is similar to that of the Phase I study, with subjects randomized 2:1 to high dose AVA-101 and control and following a similar treatment regimen and re-treatment protocols as the Phase I program. The endpoints of the study include safety and efficacy endpoints similar to the Phase I program as well. As stated earlier, the trial expects to report top-line data in the first half of 2015. Pending positive Phase IIa data, Avalanche plans to conduct a Phase IIb trial in 120 subjects in the second half of 2015. Furthermore, the patients for the Phase IIb trial will include U.S. patients, a differentiation from the Phase I and Phase IIa trials that were and are being conducted at the Lions Eye Institute in Perth, Australia.

Other Pipeline Compounds

Avalanche has several other pipeline compounds in preclinical development that the company hopes to ramp up into clinical trials in the next few years.

In-Licensed Technology From U.C. Berkeley
In May 2010, Avalanche entered a license agreement with the University of California at Berkeley (Regents) relating to "the use of recombinant gene delivery vectors for treating or preventing diseases of the eye to develop, make, have made, use, offer for sale, import, export, and sell products covered by such patent rights in all fields of use in the United States." The AAV technology used by Avalanche has the ability to generate a wide array of variants because of the directed evolution platform that has the potential to reach deeper layers of the retina, target photoreceptors, and be unrecognizable by the immune system.

Under the agreement, the company is required to proceed with the development, manufacture, and sale of the licensed products with obligations to meet certain development-stage milestones within specified periods. The company also has the right and option to extend the date of any milestones by six months up to two times by paying an extension fee. Avalanche has paid an initial licensing fee and is required to make an annual fee payment as well as development milestone payments for up to three indications. Lastly, the company must pay a low-single-digit royalty on net sales of the licensed products subject to a minimum annual royalty payment and is obligated to pay a midteens percentage of nonroyalty licensing revenue from sublicensees.

AVA-201 for Prevention of Wet AMD

AVA-201 is the company's next-generation anti-VEGF gene therapy pipeline candidate that delivers the same sFlt-1 expressing gene as AVA-101 but uses a next-generation AAV vector delivery. The product is administered by an intravitreal injection and can overcome the physical barrier presented by the anatomy of the retina, leading to transduction in retinal cells. The intention for this product is for prophylaxis use in patients with earlier forms of AMD.

The company tested whether sFlt-1 could prevent the onset of wet AMD in a preclinical study in a nonhuman primate model. Primates were transduced in one eye with a control vector in their other eye; at 16 months, choroidal neovascularization (CNV) was induced by laser irradiation and assessed at two to four weeks. Forty-six percent of the control eyes developed lesions, whereas no eyes treated with AVA-201 developed lesions. This study demonstrated that upregulation of sFlt-1 could prevent the development of CNV, which could be a preemptive measure to prevent wet AMD development.

AVA-311 for Juvenile X-Linked Retinoschisis

Juvenile X-linked retinoschisis (XLRS) is an inherited retinal disease that occurs almost exclusively in males (because of the presence of only one X chromosome), caused by mutations in the RS1 gene on the X chromosome. The protein encoded by the RS1 gene binds to the surface of the photoreceptors in the retina, and disruption in its production might cause splitting of retinal layers and/or leakage in the blood vessels of the retina. This leakage can lead to severe vision impairment or blindness and can also occur early in childhood. According to the National Institutes of Health, XLRS is estimated to affect 1 in 5,000 to 1 in 25,000 males worldwide.

In collaboration with Regeneron Pharmaceuticals, AVA-311 is being developed to include an AAV that intravitreally delivers the RS1 gene to the eye for a potentially functional cure for XLRS. In a preclinical study in a mouse model that mimics XLRS, mice were given a single intravitreal injection and monitored for four months. Treated eyes exhibited significant improvement in function after one month and the improvement was maintained over the four-month monitoring period, whereas untreated eyes had less retinal function and continued to decline over the four-month monitoring period. As part of the agreement, Regeneron has the option to be responsible for all preclinical studies and clinical trials with AVA-311 and to retain commercial worldwide rights; Avalanche has the option to share up to 35% of the development costs and profits.

Intellectual Property

The license for technology from UC Berkeley is expected to expire in 2020 unless a term extension is obtained. The company's exclusive license to a U.S. patent having composition-of-matter claims on expression vectors that encode a soluble VEGF inhibitor is expected to expire in 2015. Beyond this initial patent, however, the company has built out a portfolio with one patent family projected to expire in 2024 (Australia, Germany, France, United Kingdom, and Spain) and another patent family projected to expire in 2027 (Europe). The company expects some form of patent protection to run through 2033.

Avalanche also expects market access and exclusivity for AVA-101 with a broad issued method claim, specific claims on AVA-101 product compositions, and U.S. and worldwide filings. In addition, the AAV platform has multiple issued and pending U.S. and worldwide filings, as well as exclusivity on key AAV compositions of matter. For example, U.S. patent 6,943,153 is for the claim of "a method of inhibiting angiogenesis in a diseased eye of a subject, comprising, administering intraocularly a recombinant adeno-associated virus (rAAV) gene delivery vector which directs the expression of an anti-angiogenic factor, such that administration of said vector inhibits neovascularization of the diseased eye."

Wet AMD Competitive Landscape

In addition to the products currently on the market to treat wet AMD (Lucentis, Eylea, and off-label Avastin), several companies are trying to develop next-generation products to capture the growing retinal disease market. This should make for an interesting environment over the next several years, with Lucentis beginning to come off patent in 2018 in Canada and 2020 in the United States. We believe that the most direct competitor to Avalanche's AVA-101 is the Sanofi/AGTC product AAV2-sFLT01, which is being assessed in Phase I trials.

AAV2-sFLT01 by Sanofi/AGTC Represents Another Gene Therapy Candidate
Applied Genetic Technologies Corporation (AGTC) is a clinical-stage biotechnology company developing AAV-based gene therapies to treat eye diseases. In 2004, the company entered a collaboration with Genzyme (now Sanofi) to develop an AAV to treat wet AMD. In March 2010, the companies began a Phase I trial and the collaboration became a license agreement in which Genzyme is now fully responsible for development of the product. In December 2013, the license agreement was altered to terminate the exclusive license for Genzyme to use AGTC's HSV-based manufacturing technology. A major difference between the Sanofi/AGTC compound, AAV2-sFLT01, and AVA-101 is the injection point. AVA-101 is an intraretinal injection, whereas AAV2-sFLT01 is an intravitreal injection.

According to clinicaltrials.gov, AAV2-sFLT01 is involved in an ongoing Phase I study in 34 patients. The study involves four arms: 2×10^8 vector genomes AAV2-sFLT01, 2×10^9 vector genomes AAV2-sFLT01, 6×10^9 vector genomes AAV2-sFLT01, and 2×10^{10} vector genomes AAV2-sFLT01. The primary outcome measures are the maximum tolerated dose (MTD) of a single intravitreal injection at week 52 and the number of treatment emergent adverse events at week 52 and up to four years in an extended follow-up period. We expect the company to report preliminary data at the Retina Society annual meeting in Philadelphia on September 13 in a presentation titled, "Preliminary Results of Phase I Study With AAV2-sFLT01 as Gene Therapy for Treatment of Exudative AMD" by Dr. Jeffrey Heier.

In addition to the wet AMD compound that the company no longer has much leverage with, AGTC's lead compound is being developed to treat XLRS and the company plans to file an investigational new drug (IND) application and start a Phase I/II trial in late 2014 with initial clinical data in mid-2015. We will continue to monitor this company's progress in relation to Avalanche because of the similarities in treatment delivery technology.

DARPin for Treatment of Wet AMD Is Allergan's Highly Touted Pipeline Candidate in Its Hostile Takeover Battle With Valeant Pharmaceuticals
Abicipar pegol, or anti-VEGF DARPin, for the treatment of wet AMD, has been proclaimed by Allergan to be one of its biggest pipeline opportunities. Data released recently from stage 3 of the Phase II trial showed that patients who received doses of abicipar pegol at 1 mg (N=25) or 2 mg (N=23) had a mean visual acuity improvement from baseline after 16 weeks of 6.3 letters and 8.2 letters, respectively. This compared with the Lucentis-treated group (N=16), which showed an

improvement of only 5.3 letters. Results were expected to improve with duration of the trial. At week 20, the mean visual acuity improvement from baseline for Lucentis and 1 mg and 2 mg doses of abicipar pegol were 4.7 letters, 7.1 letters, and 9.0 letters. However, the study was not powered to detect statistical significance, and two patients in the 2 mg group and three patients in the 1 mg group experienced ocular inflammation.

In addition, Allergan created a new manufacturing process that it believes will reduce inflammatory adverse events. The Phase III program will compare abicipar pegol at 2 mg dosed every 8 weeks versus abicipar pegol at 2 mg every 12 weeks versus Lucentis every 4 weeks. Aside from the inflammation, efficacy results from abicipar pegol were impressive, especially given the improvement between weeks 16 and 20. However, the questions will likely remain as Phase III trials begin concerning the ability of the new manufacturing process to reduce inflammation and whether this new process might affect the efficacy results.

According to Allergan's projections, the global retina market could grow to $10 billion by 2019 with a CAGR of 15% from $2.5 billion in 2009. Furthermore, the company projects that DARPin could provide a best-in-class treatment duration profile to capture market share from current market leaders Lucentis from Roche (56% market share) and Eylea from Regeneron (43% market share) for around $20 billion in potential cumulative 10-year sales. Allergan plans to initiate a Phase III study in the second quarter of 2015. In addition, as part of Valeant's hostile takeover bid, the company included a $25 per share contingent value right for the potential of DARPin.

While we believe that DARPin appears to be an effective and interesting agent in development, the program has had setbacks in Phase II and we believe the once-every-three-months goal is not certain for the program. However, the commitment by Allergan to develop an AMD program is obvious, and we believe the company would likely be an interested party in partnership discussions if the AVA-101 Phase IIa program continues to suggest a curative benefit.

Lucentis Biosimilar by Pfenex Slated to Launch in Line With Lucentis Patent Expiry
A recent IPO, Pfenex, is developing a Lucentis biosimilar called PF582 that is undergoing a Phase Ib/IIa clinical trial, with a Phase III trial expected to start in mid-2015 pending positive results. With Lucentis patents beginning to expire in Canada in 2018 followed by the patents in the United States expiring in 2020, the development timelines for PF582 correspond with these patent expirations. A low-cost Lucentis biosimilar entering the market might provide further competition in the retinal disease space.

Platelet-Derived Growth Factor Is an Intriguing Target for Wet AMD; However, Therapies Are Likely to Be Dosed in Combination With VEGF Therapies
Phase IIb data from an aptamer targeting platelet-derived growth factor (PDGF), Fovista, being developed by Ophthotech Corporation, has been impressive and should be the next meaningful step in AMD therapy when used in combination with anti-VEGF therapies such as Lucentis. In a Phase IIb study of 449 patients, the patients showed an improvement of 10.6 letters in visual acuity after treatment with a combination of Fovista and Lucentis versus a gain of 6.5 letters after treatment with Lucentis alone, a 62% comparative improvement. In addition, Ophthotech has entered a licensing and commercialization agreement with Novartis, granting the latter exclusive rights to commercialize Fovista in markets outside the United States. Ophthotech has initiated a pivotal Phase III program to evaluate the safety and efficacy of Fovista and Lucentis versus Lucentis alone. According to clinicaltrials.gov, one Phase III study to establish safety and efficacy is enrolling 622 patients randomized one-to-one in a Fovista (1.5 mg per eye) plus Lucentis (0.5 mg per eye) group or sham plus Lucentis group. The primary outcome of the study is the mean change in visual acuity after 52 weeks, and the estimated completion date is July 2016. The other Phase III trial currently enrolling (also expected to read out in July 2016) is recruiting 622 patients randomized one-to-one in a Fovista (1.5 mg per eye) plus Avastin (1.25 mg intravitreal injection) or Eylea (2 mg intravitreal

injection) versus sham plus Avastin or Eylea. Lastly, the company is enrolling a Phase IIa two-year open-label safety study of Fovista administered in combination with anti-VEGF, expected to read out in April 2017.

Regeneron is also developing an anti-PDGF candidate for combination use with Eylea. According to clinicaltrials.gov, the company is recruiting a Phase I study to assess the safety of four different doses of intravitreal injections of REGN 2176-3 in 24 patients. The study is estimated to read out in February 2015.

Key Management

Avalanche Biotechnologies' management team has a range of experience in the fields of ophthalmology and gene therapy; the company's chief medical officer, Samuel Barone, M.D., previously worked at the Food and Drug Administration. Several key members have joined the team in the past year, including Dr. Barone and CFO Linda Bain, and the company also has four non-employee directors, two of whom are Avalanche co-founders. In particular, we believe that CEO Thomas Chalberg's depth of experience with Lucentis and Avastin, as well as his research training in retinal diseases and new gene therapy technology, will prove a major positive through the development of Avalanche Biotechnologies' potentially disruptive clinical programs.

Thomas W. Chalberg, Ph.D., president, chief executive officer, and director. Dr. Chalberg is a co-founder of Avalanche Biotechnologies, has been on the board of directors since 2006, and has been president and CEO since 2010. From 2005 through 2010, Dr. Chalberg held a number of roles in ophthalmology and oncology at Genentech, including leading the Lucentis strategy team, acting as senior manager of market development for Lucentis and Avastin, and leading global business at Lucentis. From 2001 through 2005, Dr. Chalberg was a Howard Hughes Medical Institute fellow at Stanford University, and he holds a doctorate in genetics from Stanford University School of Medicine, an M.B.A. from the Haas School of Business at the University of California, Berkeley, and a bachelor's degree in biomedical sciences from Harvard University.

Linda C. Bain, chief financial officer. Ms. Bain became the CFO of Avalanche in April 2014. Before joining the company, she held various roles for the gene therapy biotechnology company bluebird bio, including chief accounting officer, vice president of finance and business operations, and treasurer, from 2011 through 2014. Ms. Bain also served as the vice president of finance for Genzyme from 2008 through 2011 and in various roles at AstraZeneca from 2000 through 2007. She received a bachelor's degree in accounting and business administration as well as an honors degree in accounting and business administration from the University of the Free State in South Africa. Ms. Bain is also a certified public accountant.

Samuel B. Barone, M.D., chief medical officer. The company's most recent hire, Dr. Barone was brought onto the company's management team in June 2014. From 2009 through 2014, Dr. Barone served as a medical officer in the office of cellular, tissue, and gene therapies at the FDA. He has a wide range of experience in the field of ophthalmology, having practiced at eyecare provider Retina Associates, P.C., from 2010 through 2014; serving as a staff physician practicing ophthalmology at the VA Medical Center in San Diego; and completing a residency at the New York Eye and Ear Infirmary of Mount Sinai as well as a medical and surgical retina fellowship at the University of California, San Diego. Dr. Barone received his medical degree from Penn State College of Medicine and his bachelor's degree in biology from Boston College.

Mehdi Gasmi, Ph.D., vice president, pharmaceutical development. Dr. Gasmi has been with Avalanche since 2013 and is involved with the manufacture and quality control of the gene therapy candidates. Prior to his role with the company, Dr. Gasmi provided AAV and lentiviral gene therapy

consulting services to various companies (including Avalanche) as principal of Clinvec Solutions, L.L.C. In addition, Dr. Gasmi oversaw the production of clinical batches of AAV and gene therapy products at both Généthon (from 2009 through 2011) and Ceregene (from 2001 through 2009). Dr. Gasmi received his master's and doctoral degrees in biochemistry from Claude Bernard University in Lyon, France.

Hans P. Hull, J.D., vice president, legal and corporate development. Mr. Hull has served in his current role with the company since 2012. From 2008 through 2011, he served as a legal and business development consultant for life sciences companies, and before that he was a general manager and CEO for Orthobond Corporation, a medical device company. Mr. Hull also worked as an attorney at Heller Ehrman White & McAuliffe L.L.P. from 2003 through 2005. He received his law degree from Boalt Hall at the University of California, Berkeley, and his bachelor's degree in chemistry from Princeton University.

Mark S. Blumenkranz, M.D., director and co-founder. Dr. Blumenkranz has served as a member of the board of directors since the company's inception in July 2006 and is also a co-founder. He is a trained vitreoretinal surgeon and chairman of the department of ophthalmology at the Byers Eye Institute at Stanford University. Dr. Blumenkranz received his M.D. and M.M.S. degrees in biochemical pharmacology as well as his bachelor's degree from Brown University, followed by a residency in ophthalmology at Stanford.

Steven D. Schwartz, M.D., director and co-founder. Dr. Schwartz has served as a member of the board of directors since 2010 and is also a co-founder of the company. He is the Ahmanson Professor of Ophthalmology at the Jules Stein Eye Institute at the University of California, Los Angeles. Dr. Schwartz completed his residency in ophthalmology at the University of California, Los Angeles, and a vitreoretinal fellowship at Moorfields Eye Hospital in London. He received his M.D. from the Keck School of Medicine at the University of Southern California and his bachelor's degree from the University of California, Berkeley.

Financial Overview

Income Statement

The performance of shares of Avalanche will largely be driven in the near term by the upcoming Phase IIa data set from the company's main pipeline asset, AVA-101. Given the early stage of development for the company, we believe a product launch will not occur until 2019 at the earliest (which we model); however, this may slip into 2020 dependent on the timing of the initiation and enrollment of the company's Phase III pivotal studies.

Until then, we expect the company to ramp up research-and-development spending, from $7 million this year to over $22 million in 2015, with measured yearly growth until the company initiates its Phase III program in the second half of 2017. We believe a major swing factor in spending will likely be if Avalanche's management decides to execute a development partnership agreement in 2015 following the data readout from the company's Phase IIa study. While Regeneron holds the rights to look at this data and enter discussions for partnering for AVA-101, the company does not hold an option to in-license the program and Avalanche management has freedom to turn down any offer Regeneron proposes. While some might view the right by Regeneron to enter partnering discussions versus an in-license option as splitting hairs, we believe Avalanche remains in a strong bargaining position against its much larger and cash-rich development partner. We believe management, if it chooses to pursue a partner, should be able to execute an attractive deal for AVA-101 if data in the Phase IIa trial were to look similar in efficacy (particularly without the need for retreatment) to the Phase I data set.

Aside from research-and-development spending, the company will likely have single-digit general-and-administrative spending levels until the need for commercialization arises, which we do not expect to occur until late 2019 or 2020. Considering the unique gene therapy nature of Avalanche's product pipeline and the one-time dosing of the therapies, we anticipate gross margin to be impressive; we forecast 90%, although this may be conservative. These spending estimates suggest net losses between 2014 and 2018, with Avalanche not set to turn profitable until 2019, aside from one-time cash inflows from partnerships. While estimates so far out in time are often directional at best, we project $0.38 in earnings in 2019, which should ramp up to our initial fully taxed 2020 estimate of $9.53.

Balance Sheet Solid After Successful IPO

We estimate that Avalanche holds roughly $150 million in cash on its balance sheet, following a successful public offering in which the company priced shares at $17, at the top end of the range initially set at $13-$15, raising over $100 million. The successful IPO followed a successful series B round, which raised $55 million earlier in the year. While profitability is some ways off and we understand development timelines often change in this industry, we estimate that the company will need roughly $130 million in cash before breaking into profitability. And while development-stage companies often raise additional funds opportunistically, we believe the company's successful IPO and partnership with Regeneron for additional pipeline products has reduced that need in the near term. However, our estimates include another raise of about $60 million during 2016 to be conservative. As we noted above, management is guiding to a partnership for additional development of AVA-101, which should reduce the company's cash needs.

Because Avalanche is relatively young for a public company, its net operating loss approximates only $5 million. However, the company's closest development peer, Ophthotech, is two years away from profitability and holds a net operating loss of $86 million on its balance sheet. As Ophthotech waited until it was well into its Phase III program for Fovista before it signed a development partnership, we believe the cash utilization between Avalanche and Ophthotech will have a different trajectory.

Exhibit 35
Avalanche Biotechnologies, Inc.
Income Statement Earnings Model

8/25/14
($ in millions except EPS data)

	2012(A)	2013(A)	Q1(A)	Q2(E)	Q3(E)	Q4(A)	2014(E)	2015(E)	2016(E)	2017(E)	2018(E)	2019(E)	2020(E)	2021(E)	2022(E)
AVA-101	-	-	-	-	-	-	-	-	-	-	-	141,336	713,747	1,227,646	1,380,473
AVA-201	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AVA-311	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
License revenue	30	480	30	30	30	30	120	120	-	-	-	-	-	-	-
Grant revenue	-	-	-	-	-	-	-								
Total Revenue	30	480	30	30	30	30	120	120	120	-	-	141,336	713,747	1,227,646	1,380,473
yr/yr growth	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	72.0%	12.4%
q/q growth			NA	NA	NA	NA									
incremental rev q/q															
Cost of Goods Sold	-	-	-	-	-	-	-	-	-	-	-	56,534	71,375	98,212	110,438
Gross Profit	30	480	30	30	30	30	120	120	120	-	-	84,802	642,373	1,129,434	1,270,035
R&D	1,310	2,151	910	1,300	2,000	2,700	6,910	22,458	25,826	18,078	36,157	43,388	57,100	61,382	62,121
Growth			-	-	-	-	221%	225%	15%	-30%	100%	20%	15%	15%	15%
SG&A	536	1,783	726	1,000	1,000	1,200	3,926	6,871	7,558	8,313	9,145	36,578.54	107,062	147,317	179,461
Growth							30%	75%	10%	10%	10%	300%	100%	50%	15%
Total Operating Expenses	1,846	3,934	1,636	2,300	3,000	3,900	10,836	29,328	33,384	26,392	45,301	79,966	164,162	208,700	241,583
growth			NA	NA	NA	NA	175%	171%	14%	-21%	72%	77%	105%	27%	16%
Operating Income	(1,816)	(3,454)	(1,606)	(2,270)	(2,970)	(3,870)	(10,716)	(29,208)	(33,264)	(26,392)	(45,301)	4,835	478,211	920,734	1,028,452
EBIT Margin							NM	NM	NM	NM	NM	NM	67%	75%	75%
growth y/y (%)			NA	NA	NA	NA	NM	NM	NM	NM	NM	NM	NM	NM	NM
Depreciation and Amortization	-	-	-	250	250	250	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
Interest income	(8)	(73)	(14)												
Other income (expense)	7	(96)	(43)	750.0	750.0	750.0	3,000	2,000	1,500	1,500	8,000	8,000	8,000	8,000	8,000
Change in fair value of embedded derivative	6	18	-												
Loss on extinguishment of conv. notes	-	(1,671)	-												
Total other (expense) income, net	5.0	(1,822)	(57)												
Income Before Taxes	(1,811)	(5,276)	(1,663)	(1,520)	(2,220)	(3,120)	(8,523)	(27,208)	(31,764)	(24,892)	(37,301)	12,835	486,211	928,734	1,036,452
Income Tax Provision	-	-	-	76	225	225	526	1,000	1,000	-	-	-	165,312	315,770	352,394
Effective Tax Rate	0.0%	0.0%	NA	5.0%	NA	NA	NM	NA	NA	0%	0%	0%	34%	34%	34%
Foreign currency adjustment	8.0	19.0													
Net Income (loss) Attributable to Common	(1,803)	(5,257)	(1,663)	(1,596)	(2,445)	(3,345)	(9,049)	(28,208)	(32,764)	(24,892)	(37,301)	12,835	320,899	612,965	684,058
Net income to common per share (diluted)	$ (0.50)	$ (1.44)	$ (0.45)	(0.08)	(0.09)	(0.13)	(0.37)	(0.97)	(1.02)	(0.76)	(1.14)	0.38	9.53	18.14	20.19
Basic avg. number of shares used in computing net income	3,643	3,673	3,673	18,691	22,257	22,357	21,102	24,857	26,007	26,407	32,641	32,741	32,841	32,941	33,041
Diluted avg. number of shares used in computing net income	3,643	3,673	3,673	20,114	26,391	26,491	24,332	28,991	32,141	32,541	32,641	33,585	33,685	33,785	33,885
Key Ratios (GAAP unless noted)															
Gross Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	90.0%	50.0%	60.0%	90.0%	92.0%	92.0%
R&D (% Total Rev.)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	30.7%	8.0%	5.0%	4.5%
SG&A (% Total Rev.)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	25.9%	15.0%	12.0%	13.0%
Operating Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	3.4%	67.0%	75.0%	74.5%
Net Income Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	9.1%	45.0%	49.9%	49.6%
Revenue Growth															
Growth Yr/Yr	NM	1500%	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	405.0%	72.0%	12.4%
Growth Q/Q	NM		NM	NM	NM	NM									
SG&A Growth															
Growth Yr/Yr	NM	233%	NM	NM	NM	NM	120%	75%	10%	10%	10%	300%	193%	38%	22%
Growth Q/Q	NM		NM	NM	NM	NM									
R&D Growth															
Growth Yr/Yr	NM	64%	NM	NM	NM	NM	221%	225%	15%	-30%	100%	20%	105%	27%	16%
Growth Q/Q	NM		NM	NM	NM	NM									

Sources: William Blair & Company estimates and Company reports

Valuation and Stock Thoughts

Shares of Avalanche have performed well since the company priced its initial public offering at $17, above the offering range. Shares have appreciated roughly 80% since the IPO, which we believe is based on investor appetite for a potentially disruptive product in a large market with a platform technology capable of organically adding to the company's pipeline. Despite the stock appreciation, we believe shares of Avalanche continue to hold an asymmetric risk/reward profile, given the past success companies have had in reducing the dosing frequency for AMD therapies. We believe Avalanche's therapy holds clinical risk; however, the upside potential for AVA-101 in becoming a curative therapy in AMD suggests that the upside to Avalanche shares is significant. While it is unlikely that the company will become the next Regeneron, Avalanche shares trading at 5% of the value of Regeneron's market cap still suggest a greater-than-330% appreciation from current levels.

We are establishing a price target of $52, based on a net present value of the company's lead development program, AVA-101. In this calculation, we assume a launch of AVA-101 in 2019 following approval early that same year. We believe peak-year sales will approximate $1.1 billion domestically. Eylea sales as of the second quarter are annualizing at a $1.66 billion run-rate less than three years into its launch despite competition from Lucentis and off-label compounded Avastin use. Our estimates assume a penetration of 45% into the AMD incidence and a cost of $30,000 (below the $44,000 to $46,000 cost of two years of Lucentis/Eylea), we also include minimal revenue from DME and RVO, and no revenue from outside the United States, which is likely conservative. Given the success of Eylea, which is set to be a $1.6 billion drug only three years after approval, we view AVA-101 as holding an asymmetric risk/reward profile, with the product either having the potential to become a blockbuster or not succeeding in clinical development or approval. Appendix C includes our market build for AVA-101. Our valuation excludes other pipeline compounds, such as AVA-201, AVA-311, and the company's additional pipeline products being developed with Regeneron, which might lead to eight additional compounds. We include our risk-adjusted net-present-value breakdown for Avalanche shares in exhibit 36.

Exhibit 36
Avalanche Biotechnologies, Inc.
Sum of the Parts Valuation

	Peak Sales	Discount Rate	Probability of Success	Peak Sales	Value Per Share
AVA101	$1,136	11%	50%	2024	$ 46.58
Cash Per Share					$ 5.68
NPV Value					$1,229,183
NPV Value Per Share					$ 52.26

Source: William Blair & Company L.L.C. estimates

In exhibit 37, on the following page, we provide the enterprise values of other development companies that have a clear overlap with Avalanche. These include either Phase III data in hand or recently approved therapies. While the closest comparable is Ophthotech, with an enterprise value around $1 billion, we still view the roughly $494 million enterprise value of Avalanche as attractive. Mean comparable enterprise values, which we include in our comparable analysis (exhibit 37), suggest a potential enterprise value of $544 million for ophthalmology and gene therapy assets. This implies a discount to this group alone. Given this discount to Ophthotech and the company's peer group, we believe shares should trade well pending positive Phase IIa data in early 2015.

Exhibit 37
Avalanche Biotechnologies, Inc.
Opthomology and Gene Therapy Comparable Companies

Company	Ticker	Price	Rating	Market Capitalization	EV
Opthotech Corp.	OPHT	$36.51	Not Rated	$1,179	$926
Sangamo Biosciences	SGMO	$13.27	Not Rated	$839	$625
bluebird bio	BLUE	$35.51	Not Rated	$857	$665
Avalanche Biotechnologies	AAVL	$30.15	Outperform	$644	$494
Aerie Pharmaceuticals	AERI	$16.87	Not Rated	$400	$335
Applied Genetic Tech.	AGTC	$18.43	Not Rated	$257	$210
Average				$706	$543

Source:FactSet estimates

Stock Performance

The performance of Avalanche shares, up 77% since the company priced its IPO on July 31 at $17 per share, has been impressive, compared with the S&P 500 decline of 0.7% and the Nasdaq Biotechnology Index decline of 1.6% over the same period. Despite a recent sell-off in the sector, likely because of a more-risk-averse overall market, year-to-date performance for biotechnology and development-stage pharmaceutical companies continues to be strong, with the Nasdaq Biotechnology Index up 12.3% versus the S&P 500 up 6.14% year to date. Based on our belief that Avalanche is developing a potentially groundbreaking therapy in a large market, we believe shares will significantly outpace market returns if the upcoming Phase IIa study set to report out in 2015 continues to suggest AVA-101 is safe and effective. Beyond the company's Phase IIa study, we believe proofs of concept from other pipeline therapies being developed by Avalanche along with Regeneron will likely serve as additional validations of the company's technology and also serve as catalysts for shares.

Conclusion

Avalanche is developing a potentially disruptive product in AVA-101 that has the potential to functionally cure wet AMD, a leading cause of blindness. We believe the market for retinal diseases is significant and continues to grow, and the company's proprietary Ocular BioFactory platform represents significant upside as the company expands its pipeline of gene therapy products. The total addressable market for wet AMD approximates 150,000 new patients per year, with about 103,000 new drug-treated eyes each year. Our estimates assume approval and launch of AVA-101 in 2019 with peak sales exceeding $1.1 billion domestically through penetrating only 45% of newly diagnosed patients.

Based on our belief that AVA-101 represents a potentially game-changing therapy for a growing ocular disease market, we are initiating coverage with a $52 price target, Outperform rating, and Aggressive Growth company profile.

Appendix A
Avalanche Biotechnologies, Inc.
Products for Wet Age-Related Macular Degeneration in the Market or Under Development

Company	AMD Drug	N	Efficacy
Regeneron	Eylea	VIEW 1: 1217 VIEW 2: 1240	Week 96: 7.6 letters, week 52: 8.4 letters, 11.2 injections over two years, 4.2 injections during the second year Proportion of patients who required frequent injections (6+) during the second year: 15.9% Eylea 2 mg 8-week versus 26.5% ranibizumab Average of 1.4 fewer injections in the second year compared with the ranibizumab group (6.6 versus 8.0)
Regeneron	REGN 2176-3	24	NA
Roche	Lucentis	550 716 423	11.3 mean injections, +10.1 letters, 7.7 mean injections, +8.2 letters Mean change in visual acuity from baseline over 24 months was 21.5 :+6.6 in Lucentis-treated (n=240) vs. -14.9 in sham (n=238) Mean change in visual acuity from baseline over 24 months was 20.5: +10.7 in Lucentis-treated (n=139) vs. -9.8 in verteporfin PDT (n=143)
Opthotech	Fovista	449	Week 24: 10.6 letters with Fovista/Lucentis versus 6.5 letters at baseline
Allergan	DARPin	abicar pegol 2mg, n=23 1 mg, n=25 Lucentis 0.5mg, n=16	Week 16 abicipar pegol 2mg: 8.2 letters of improvement abicipar pegol 1mg: 6.3 letters of improvement Lucentis: 5.3 letters of improvement Week 20 abicipar pegol 2mg: 9.0 letters of improvement abicipar pegol 1mg: 7.1 letters of improvement Lucentis: 4.7 letters of improvement

Sources: Company reports and William Blair & Company, L.L.C.

Appendix B
Avalanche Biotechnologies, Inc.
Most Common Adverse Reactions in Lucentis and Eylea in AMD, DME, and RVO Studies

Adverse Reactions	Wet-AMD			AMD (2-year)			AMD (1-year)			CRVO			RVO (6-month)			DME			DME (2-year)		
	Eylea	Ranibizumab	Change	Lucentis	Control	Change	Lucentis	Control	Change	Eylea	Control	Change	Lucentis	Control	Change	Eylea	Control	Change	Lucentis	Control	Change
Conjuctival hemmorhage	25%	28%	-3%	74%	60%	14%	64%	50%	14%	12%	11%	1%	48%	37%	11%	28%	17%	11%	47%	32%	15%
Eye pain	9%	9%	0%	35%	30%	5%	26%	20%	6%	13%	5%	8%	17%	12%	5%	9%	6%	3%	17%	13%	4%
Vitreaous floaters	6%	7%	-1%	27%	8%	19%	19%	5%	14%	5%	1%	4%	7%	2%	5%	6%	3%	3%	10%	4%	6%
Vitreous detachment	6%	6%	0%	21%	19%	2%	15%	15%	0%	3%	4%	-1%	4%	2%	2%	3%	3%	0%	11%	15%	-4%
Intraoccular pressure	5%	7%	-2%	18%	8%	10%	13%	7%	6%	8%	6%	2%	7%	2%	5%	5%	3%	2%	18%	7%	11%
Cataract	7%	7%	0%	17%	14%	3%	11%	9%	2%	NA	NA	NA	2%	2%	0%	8%	9%	-1%	28%	32%	-4%

Sources: Regeneron and Roche company reports

Appendix C
Avalanche Biotechnologies, Inc.
AVA-101 Market Model

AVA-101 Market Model	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
U.S. Population	316,128,839	319,290,127	322,483,029	325,707,859	328,964,938	328,964,938	332,254,587	335,577,133	338,932,904	342,322,233
% of population 65 years of age and older (1)	14%	14%	14%	14%	14%	14%	14%	14%	14%	14%
% Wet AMD Incidence in over 65 patient population (2)(3)	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%
U.S. population ≥65 with wet AMD	129,929	129,929	129,929	129,929	129,929	135,205	136,557	137,922	139,301	140,694
Total Eyes (incl. bilateral disease) minus treated eyes	149,418	149,418	149,418	149,418	149,418	155,485	157,040	158,611	160,197	120,877
Treatment eligible eyes	75%	75%	75%	75%	75%	75%	75%	75%	75%	75%
Total number present and treated (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
Total number present and treated	89,651	89,651	89,651	89,651	89,651	93,291	94,224	95,166	96,118	97,079
Penetration of AVA-101	0%	0%	0%	0%	0%	0%	5%	25%	43%	45%
Patients on AVA-101	-	-	-	-	-	-	4,711	23,792	40,922	43,516
Cost of AVA-101 Treatment ($000)	30	30	30	30	30	30	30	30	30	30
U.S. Sales of AVA-101 ($000)	-	-	-	-	-	-	141,336	713,747	1,227,646	1,305,473
Ex-U.S. AMD Market	3,000,000	3,000,000	3,000,000	3,000,000	3,000,000	3,000,000	3,000,000	3,000,000	3,000,000	3,000,000
Penetration into Ex-U.S. Market	-	-	-	-	-	-	-	-	-	-
Ex-U.S. Sales of AVA-101	-	-	-	-	-	-	-	-	-	-
Diabetic Macular Edema (DME) Market	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000
Penetration into DME Market	-	-	-	-	-	-	0%	0%	0%	5%
U.S. Sales of AVA-101 in DME	-	-	-	-	-	-	-	-	-	50,000
Ex-U.S. DME Market	800,000	800,000	800,000	800,000	800,000	800,000	800,000	800,000	800,000	800,000
Penetration into Ex-U.S. DME Market	-	-	-	-	-	-	0%	0%	0%	0%
Ex-U.S. Sales of AVA-101 in DME	-	-	-	-	-	-	-	-	-	-
Retinal Vein Occlusion (RVO) Market	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000
Penetration into RVO Market	-	-	-	-	-	-	0%	0%	0%	5%
U.S. Sales of AVA-101 in RVO	-	-	-	-	-	-	-	-	-	25,000
Ex-U.S. RVO Market	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000
Penetration into Ex-U.S. RVO Market	-	-	-	-	-	-	-	-	-	-
Ex-U.S. Sales of AVA-101 in RVO	-	-	-	-	-	-	-	-	-	-
Total AVA-101 Sales (U.S.)	-	-	-	-	-	-	141,336	713,747	1,227,646	1,380,473
Total AVA-101 Sales ex-U.S.	-	-	-	-	-	-	-	-	-	-
Total AVA-101 Sales	-	-	-	-	-	-	141,336	713,747	1,227,646	1,380,473
Growth Yr/Yr	NA	NA	NA	NA	NA	NA	NA	NA	72%	12%
Growth O/O	NA	NA	NA	NA						

Assumptions
(1) U.S. census population 316,128,839
U.S. census persons 65 years of age and over (13.7%)
(2) Javitt et al. Ophthalmology, 2003. 110(8); 1534-1539
(3) Beaver Dam Eye Study

Sources: U.S. Census, Javitt et al. *Ophthalmology* 2003, Beaver Dam Eye, Study

Links
http://quickfacts.census.gov/qfd/states/00000.html
http://quickfacts.census.gov/qfd/states/00000.html

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