Zacks Small-Cap Research

February 25, 2014
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iCo Therapeutics Inc.

(ICOTF:OTC)

ICOTF: Keep An Eye On iCo Therapeutics – Initiating Coverage…

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	02/25/2014
Current Price (02/25/14)	$0.38
Target Price	**$0.90**

INITIATION

We are initiating Coverage of iCo Therapeutics Inc. with an Outperform rating and $0.90 price target.

Sum-of-parts modeling calculates that iCo Therapeutics shares are meaningful undervalued at today's market value of only $30 million on a basic share count basis. We find this bafflingly low. Our analysis finds that the shares should be valued more in the $100-105 million range, or around $0.90 per share on a fully-diluted basis based on a 50% probability of success of the iDEAL trial. This represents tremendous upside to investors at today's price of only $0.38 per share.

SUMMARY DATA

52-Week High	**$0.40**
52-Week Low	**$0.35**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**61,102**
Shares Outstanding (mil)	**N/A**
Market Capitalization ($mil)	**$31**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2013 Estimate	**N/A**
P/E using 2014 Estimate	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2013	0 A	0 A	0 A	0 E	0 E
2014	0 E	0 E	0 E	0 E	0 E
2015					0 E
2016					0 E

Earnings per Share

(EPS is operating earnings before non-recurring items)

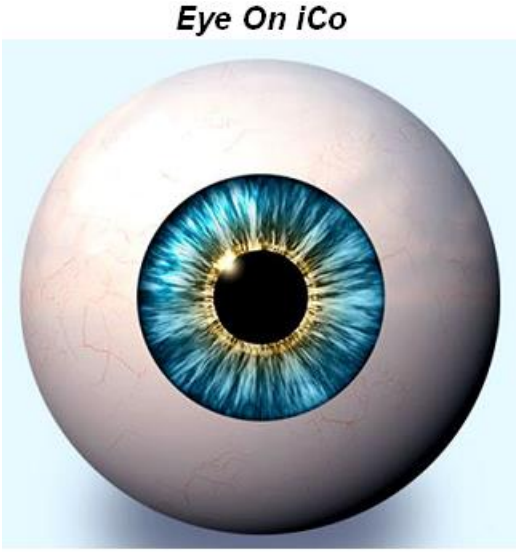
	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2013	-$0.03 A	-$0.01 A	-$0.04 A	-$0.02 E	-$0.07 E
2014	-$0.02 E	-$0.02 E	-$0.02 E	-$0.02 E	-$0.09 E
2015					-$0.03 E
2016					-$0.04 E

WHAT'S NEW

Initiating Coverage

We are initiating Coverage of iCo Therapeutics Inc. with an Outperform rating and $0.90 price target. Sum-of-parts modeling calculates that iCo Therapeutics shares are meaningful undervalued at today's market value of only $30 million on a basic share count basis. We find this bafflingly low. We note this value does not include some 28.6 million warrants at or very near in-the-money. This could add another $15 million market value, but also $11 million in cash to the company if exercised.

Our analysis finds that the shares should be valued more in the $100-105 million range, or around $0.90 per share on a fully-diluted basis based on a 50% probability of success of the iDEAL trial. This represents tremendous upside to investors at today's price of only $0.38 per share. However, investors need to be aware that approximately 80% of our valuation is coming from iCo-007 for the treatment of DME (and off-label use in AMD). Pipeline products iCo-008 and iCo-009 represent upside to our valuation, and some downside protection should iDEAL fail. We expect top-line results from the iDEAL study are expected in April 2014.



It is clear there is dramatically more upside in the shares based on the results of iDEAL than downside. We suspect that the failure of iDEAL hits the shares by 50%, whereas success could re-value them higher at 600% in time. This type of favorable risk / reward should be attractive to most investors. We believe there will be a substantial multi-month run in the shares to the full data in September / October 2014 if the top-line results in April 2014 look solid. So we would advise keeping an eye on the shares for the top-line results in April 2014. A prudent strategy might be to establish a position today, and then fill the rest of the order if the data from iDEAL is April 2014 impresses

INVESTMENT OVERVIEW

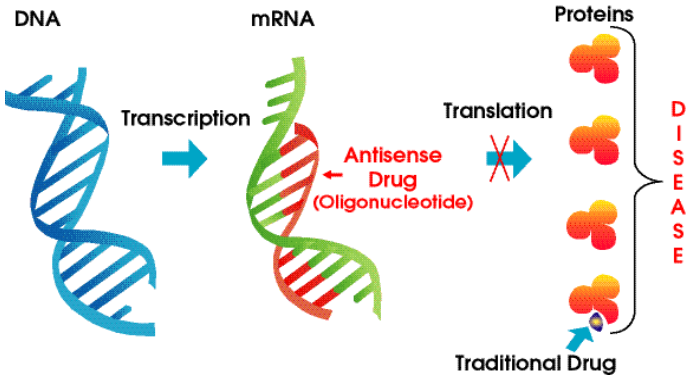
Antisense: It's Starting To Make Sense

Antisense technology came about nearly 35 years ago and was heralded as a potential major breakthrough for the pharmaceutical industry. At the time, scientists believed that antisense offered a more focused and efficient approach to drug discovery and development. For instance, it was believed that antisense drugs could be designed for specific diseases or indications without the need for inefficient and expensive screening or substantial preclinical lead optimization work. It was also believed that disease targets, previously undruggable through traditional small molecule or biologic mechanisms, would be accessible through newly developed antisense molecules.

…How Antisense Works…

The approximately 30,000 genes in the human genome can be transcribed into about 85,000 different messenger RNA (mRNA) molecules, each used in the cell as a template to synthesize a different protein. Messenger RNA, transcribed from DNA, is the genetic instructions for the production of a particular protein. Conventional pharmaceutical drugs (small molecules), peptides, proteins (hormones), and antibodies (biologics) typically bind to the target protein or receptor directly to treat a disease. Antisense drugs are designed to bind to the mRNA of a target protein, inhibiting the protein production process known as translation.

Antisense compounds are designed to have the right nucleotide base sequence to bind specifically (complementary) to and interfere with or inhibit translation of a target protein. To create antisense drugs, special chemically stabilized nucleotides are synthetically linked together in short chains of about 12-30 nucleotides (called oligonucleotides). Each antisense drug is designed with the right complementary genetic code to bind to a specific sequence of nucleotides in its mRNA target to form a short area of double strands. This double stranded region can inhibit the production of protein by a number of mechanisms.



Source: UC Davis

…A Checkered Past…

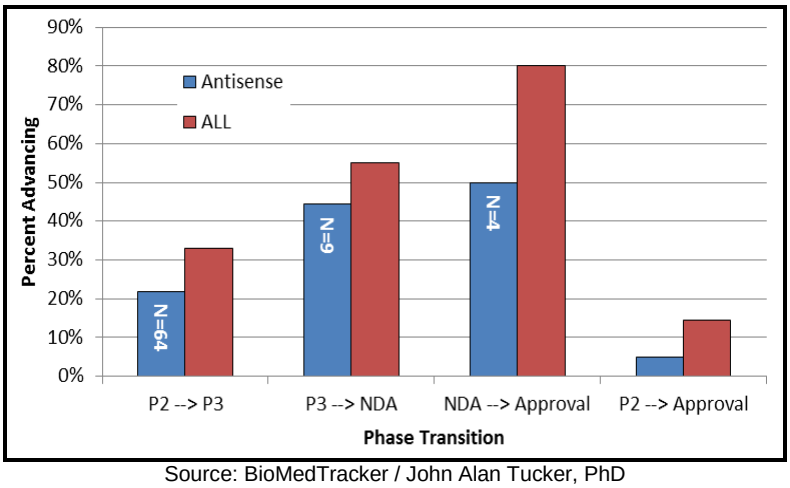
In 1991, ISIS Pharmaceuticals, the current market leader for antisense technology, filed for an IPO and commanded a market capitalization of over $400 million within six months. During the 1990's and 2000's, pharmaceutical companies spent billions attempting to develop antisense drugs. According to the BioMedTracker database, some 80 antisense compounds entered clinical development in over 140 indications between 1990 and 2010. Oddly enough, almost all these first-generation molecules failed due to enzymatic cleavage and poor circulation in the blood. Only one antisense drug, Novartis' Vitravene for cytomegalovirus (CMV) retinitis made it to the market between 1990 and 2010.

Vitravene, approved by the FDA in 1998, was discovered by ISIS Pharmaceuticals to treat CMV retinitis in AIDS patients. CMV retinitis is a viral infection of the retina. However, new anti-HIV drugs, particularly protease inhibitors and combination treatment regimens, have prolonged survival in HIV-infected individuals, resulting in a marked decline in mortality from AIDS. This was accompanied by a decline in the incidence of many opportunistic infections, including CMV retinitis. As a result, Novartis no longer markets Vitravene. Despite the lack of commercial success for Vitravene, the drugs approval demonstrated the ability of antisense technology to meet FDA and European regulatory requirements for safety and efficacy, as well as pharmaceutical company's ability to commercially manufacture antisense drugs.

We think this is of particular interest with respect to investment in iCo Therapeutics, a company whose core focus is on developing locally administered antisense drugs for ocular disease. Vitravene was a locally administered injection into the eye of the CMV affected patient. It seems clear now that much of the lack of success in first-generation antisense drug development over the past 25 years appears to have arisen from poor cell penetration and distribution properties of the drugs.

Despite the high promise for antisense drug development in the 1980's and 1990's, success in gaining approval for antisense drugs outside of Vitravene in 1998 has been low. Independent biotechnology analyst, John Alan Tucker, PhD, took a hard look at the high historical failure rate of antisense drugs over the past two decades. Dr. Tucker concludes that poor cell penetration and distribution of antisense drugs could not be compensated for by optimizing in vitro properties such as target affinity. Additionally, the analyst believes there was a remarkable insistence of moving compounds forward into advanced clinical development without early stage pharmacodynamics studies demonstrating in vivo target engagement.

According to BioMedTracker research, the historical clinical failure rate of antisense drugs is high compared to traditional small molecules and biologics. For example, between 1991 and 2010, antisense drugs had only a 5% likelihood of approval compared to 15% for all drugs under development. Likelihood of success, defined as advancement of clinical phase, was also meaningfully lower for antisense drugs when compared to all pharmaceutical drugs under development.



Source: BioMedTracker / John Alan Tucker, PhD

Dr. Tucker notes two important characteristics that may contribute to the high clinical failure rate of antisense drugs over the past two decades:

1) Failure to penetrate into the cell: One important difference between antisense drugs and traditional small molecule drugs is that antisense drugs are very large and have a large negative charge. For example, traditional small molecule drugs typically contain fewer than 60 atoms and have a net neutral charge. Thus, these molecules can travel across the cell membrane by passive diffusion. Conversely, antisense drugs may contain 700 atoms and carry a negative charge of -18 to -20. These larger and negatively charged drugs enter the cell by endocytosis, a more complex and much less efficient process. This suggests that antisense drugs may need to be present in the tissues at higher concentrations compared to a traditional small molecule drug to be equally effective.

2) Uneven distribution: Because of their high molecular weight, antisense drugs also tend to distribute unevenly in the body, with a tendency to accumulate in the liver and the proximal tubules of the kidney, and to a lesser extent in the skin, bone marrow, muscle and intestines. Low concentrations are found in other organs. Qualitatively similar but less detailed results have been observed in the clinic. A study conducted by Bijsterbosch et al published in the Oxford Journals (Vol. 25, Issue 16, pp 3290-6) found that an intravenously administered radio-labeled antisense drug accumulated mainly in the liver (roughly 41%) and the kidneys (roughly 18%). This suggests that systemic delivery of an antisense compound has little therapeutic utility unless the target organ is the liver or the kidney. Bijsterbosch et al also found that clearance from circulation of first-generation antisense drugs is rapid, with a circulating half-life of only 23 minutes in rats. The data to the right was captured only 90 minutes after intravenous injection, again suggesting that systemic delivery of antisense drugs, unless targeting the liver, is a flawed approach.

Tissue	Radioactivity (% of recovered)
Blood plasma	2.1 ± 0.3
Urine	2.5 ± 0.4
Liver	40.5 ± 1.4
Spleen	0.7 ± 0.1
Bone marrow	6.7 ± 0.7
Kidneys	17.9 ± 1.3
Intestines	6.4 ± 0.6
Pancreas	2.2 ± 4.4
Muscles	5.5 ± 0.8
Skin	8.4 ± 1.7
Carcass (including marrow)	10.4 ± 0.5
All other tissues	3.3 ± 0.1

Source: Bijsterbosch et al, 1997

…Antisense 2.0 (or 2.5) – Finally On Target…

Armed with the knowledge and experience of past failures, antisense drug development companies, ISIS Pharmaceuticals specifically, seem to have dramatically shifted focus to liver-focused or locally administered drugs. In fact, the majority of ISIS Pharmaceuticals existing development pipeline is focused on liver-specific targets or locally administered antisense drugs. For the purpose of this report, we will focus on local administration. Analysis of the BioMedTracker database suggests success rates for Phase 2 drugs (success defined as movement into Phase 3) was 60% (3 of 5) for locally administered drugs versus only 21% (14 of 68) for systemically administered drugs. Local administration of an antisense drug directly into the eye is both clinically and commercially validated by the development and approval of ISIS Pharmaceuticals' Vitravene, and its commercialization by Novartis in 1998.

The leading pipeline candidate at iCo Therapeutics, iCo-007, is second-generation locally administered antisense drug discovered by ISIS Pharmaceuticals and licensed to iCo Therapeutics in 2005 for the treatment of diabetic macular edema.

Diabetic Macular Edema

According to the American Diabetes Association, 25.8 million Americans have diabetes. A recent study out of the Singapore Eye Research Institute suggests that 7% of diabetic patients may develop diabetic macular edema (DME) or diabetic retinopathy (DR) (Ding J. et al, 2012). The risk factors for DME are largely similar to DR, but dyslipidemia appears to play a more significant role. Applying the 7% prevalence suggested by Ding J. et al pegs the U.S. DME market at around 1.8 million people. Another study out of the Lawson Health Research Institute in Canada found an approximate 15.7% prevalence of DME among diabetic patients, with 2.56% having significant visual impairment (Petrella RJ. et al, 2012). This suggest a U.S. population of nearly 4 million patients, 0.65 million with severe visual impairment.

DME occurs when blood vessels in the retina of patients with diabetes begin to leak into the macula, the part of the eye responsible for detailed central vision. These leaks cause the macula to thicken and swell, progressively distorting acute vision. While the swelling may not lead to blindness, the effect can cause a severe loss in central vision. Nevertheless, DME is the major cause of vision loss in people with diabetic retinopathy.

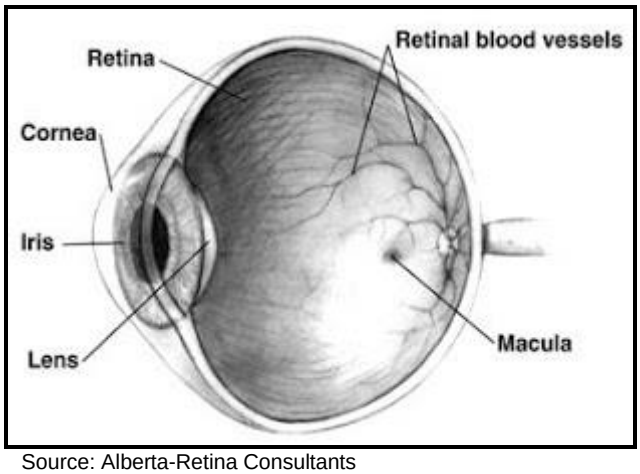
Normal Vision Illustration

Vision Loss Due to DME Illustration

Source: Genentech

The retina is the light sensitive area at the back of the eye, and the macula is the central part of the retina used for high resolution vision. In diabetes, the accumulation of metabolic products arising from the processing of excess serum glucose leads to capillary damage, which has multiple sight-threatening consequences. The leakage of damaged capillaries causes proteins and extracellular fluids to build up in the retina, leading to swelling (edema). Edema within the macula causes a blurring of vision.

Hypoxia caused by capillary damage causes the release of vascular endothelial growth factor (VEGF) and other pro-angiogenic factors. The new blood vessels formed in response are poorly formed and fragile, accompanied by fibrous supporting tissue, and may invade the vitreous fluid. Bleeding from these fragile blood vessels may create blind spots by blocking light from reaching the retina, and the fibrous support stresses the eye structure and may lead to retinal detachment and a profound loss of vision. VEGF also promotes vascular permeability, thus exacerbating macular edema.



Source: Alberta-Retina Consultants

Diabetic retinopathy becomes nearly ubiquitous with long-standing diabetes. After 20 years with the disease, 60% of Type-2 diabetics and virtually 100% of Type-1 diabetics will manifest some form of retinopathy. Alpharetta, George-based Alimera Sciences (NASDAQ:ALIM), estimated diabetics have a 10% risk of developing the condition during their lifetime; this is consistent with the data from Singapore and Canada noted above. Given the large and rapidly growing U.S. pre-diabetic population, we estimate that approximately 300,000 new cases of DME develop annually. California-based Genentech, estimates that 55% of Americans with DME are unaware they have the disease, and that 70% of the patients with diabetic retinopathy will go on to develop DME.

…Current Treatment Options…

We encourage investors to read this recent publication on Medscape.org for a more detailed explanation of current treatment options in DME.

Laser photocoagulation: The mainstay of therapy for diabetic macular edema is laser photocoagulation. Compromised spots within the blood vessels of the retina are specifically targeted with the laser, which causes clots and halts fluid leakage. Ultimately, this leads to improved oxygen supply to the retina and reduced downstream neovascularization. Microaneurysms, the sources of leakage in DME, are targeted by the laser, and hemoglobin in the microaneurysms absorbs the laser energy. This promotes thrombosis within the microaneurysm, halting further leakage. Clinical trials have demonstrated a 50% reduction in moderate to severe visual loss from DME when laser photocoagulation is initiated early in the course of the disease.

A 10-year study by the National Eye Institute called Early Treatment Diabetic Retinopathy Study (ETDRS) was designed to evaluate the effectiveness of both argon laser photocoagulation and aspirin therapy in delaying or preventing progression of early diabetic retinopathy to more severe stages of visual loss and blindness. The study was also designed to help determine the best time to initiate photocoagulation treatment, to monitor closely the effects of diabetes mellitus and of photocoagulation on visual function, and to produce natural history data that can be used to identify risk factors and test etiologic hypotheses in diabetic retinopathy. A total of 3,711 patients were followed for a minimum of 4 years to provide long-term information on the risks and benefits of the treatments under study. Results of ETDRS suggest (source: NEI/NIH, 1999):

- ✓ Aspirin use did not affect the progression of retinopathy to the high-risk proliferative stage in eyes.
- ✓ Photocoagulation reduced the risk of moderate vision loss, especially for those eyes with macular edema that involved or threatened the center of the macula. There was moderate visual gain in those eyes that received focal treatment as well as a decrease in the amount of retinal thickening.
- ✓ A statistically significant reduction in severe visual loss was found for those patients with early treatment, especially for those patients with non-insulin-dependent diabetes mellitus.

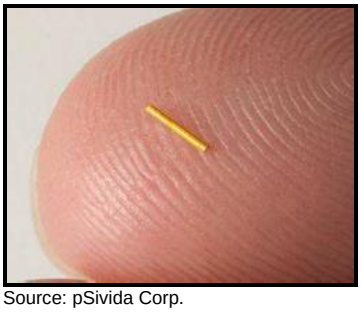
The advantages of photocoagulation have been made clear by the ETDRS. However, macular photocoagulation is not without risks. Complications of macular laser treatment include paracentral scotomas, lateral creep of juxtafoveal laser scars into the fovea, accidental foveal photocoagulation, subfoveal fibrosis, and choroidal neovascularization at the sites of laser scars. In addition, there can be residual massive hard exudates after the resolution of edema, and patients often experience color vision impairment.

In general, laser photocoagulation prevents further vision loss but does not routinely restore vision already lost to DME. As such, photocoagulation is commonly supplemented by medical treatments, among which the intravitreous administration of corticosteroids and vascular endothelial growth factor antagonists are the most widely used.

Corticosteroids: Use of corticosteroids is common in the treatment of macular edema. There are a handful of corticosteroid-based intravitreal implants under development. Products include a dexamethasone biodegradable implant (Posurdex®, Allergan), the helical triamcinolone acetonide implant (I-vation™ TA, SurModics), the fluocinolone acetonide implant (Retisert®, Bausch & Lomb), and another fluocinolone acetonide–based implant that is injectable (Medidur™, pSivida / Alimera Sciences). Although not a novel concept, drug delivery via intravitreal implant remains undesirable to patients. The advent of sustained release corticosteroids has made repeated intravitreal injections unnecessary, and thus use of corticosteroids has grown over the last decade.

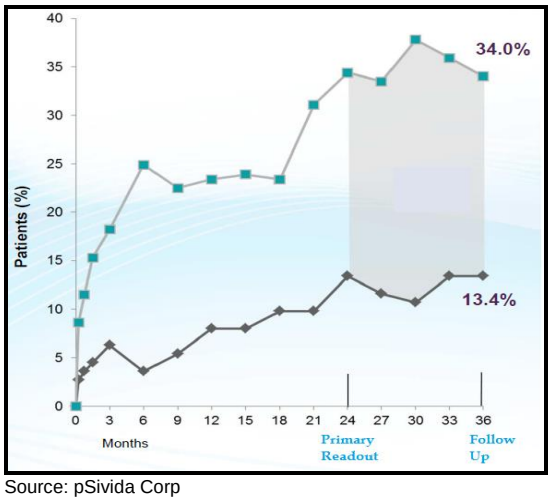
- ✓ Dexamethasone injection for the treatment of macular edema was recently evaluated in a Phase 2 trial involving 315 subjects with macular edema arising from various causes, including diabetes, central retinal vein occlusion, uveitis, and post-cataract surgery. The implant is a small biodegradable pellet injected in the operating room or the examination lane using a 20-gauge needle in sustained release over approximately one month. Results at 6 months show a gain in visual acuity of 2 or more lines was achieved in 36%, 27%, and 19% of eyes receiving the 700-mcg implant, the 350-mcg implant, and observation, respectively (p=0.008). Similarly, a gain of 3 or more lines visual acuity was achieved in 19%, 13%, and 8% of eyes, respectively (p=0.02). A statistically significant reduction in both central macular thickness and leakage by fluorescein angiography was also seen in implanted eyes versus controls, with a notable dose-response effect favoring the higher dose.
- ✓ Triamcinolone acetonide is effective in the management of macular edema because it suppresses inflammation, reduces extravasation of fluid from leaking blood vessels, inhibits fibrovascular proliferation, and down-regulates production of VEGF. However, intravitreal injection of triamcinolone is associated with significant adverse events, including elevated intraocular pressure in up to half of injected eyes and cataract formation, as well as injection-related complications such as endophthalmitis and retinal detachment.
- ✓ To overcome the issues with triamcinolone acetonide, researchers have recently focused their efforts on a helical triamcinolone implant. The drug is deposited in a proprietary polymer coating on a helical nonferrous metallic scaffold designed to maximize surface area for drug delivery while minimizing overall implant size. Its diameter is less than 0.5 mm, and it can be implanted through a small-gauge needle track via the pars plana. A Phase 1 trial involving 30 subjects with DME was recently completed showing 87% of subjects had maintained or improved visual acuity compared with baseline six months after implant. No sustained elevations of intraocular pressure were noted in the study group during the limited follow-up, and the device was well tolerated by all participants.
- ✓ Fluocinolone acetonide is a potent corticosteroid, which reduces the amount of drug required to be incorporated into the device, consequently minimizing device size. Furthermore, fluocinolone acetonide has a short half-life in the systemic circulation, reducing the likelihood of systemic side effects. The fluocinolone acetonide intravitreal implant is FDA approved for the treatment of chronic noninfectious posteriorsegment uveitis. A recent prospective, multicenter, randomized, controlled clinical trial investigated the role of the fluocinolone acetonide implant in DME patients. Results showed mixed response, with little difference in visual acuity levels between eyes that received the implant and eyes that received SOC treatment at 12 months, and moderate to significant improvement at 24 and 36 months, respectively. We discuss Iluvien™ below.

Iluvien™ (fluocinolone acetonide) is a drug-device combination product approved in the UK, Austria, France, Germany, Portugal, and Spain for the treatment of DME. Iluvien™ is an injectable, non-erodible, intravitreal implant for the treatment of DME that works by slowly releasing the corticosteroid drug fluocinolone acetonide for up to three years after implant. The device is designed to be small enough to be injected into the back of the eye with a 25 gauge needle creating a self-sealing hole. This insertion procedure is very similar to an intravitreal injection for other AMD or DME products. Iluvien™ has been rejected by the U.S. FDA on three separate occasions, the third and most recent of which took place in October 2013 and seemingly killed the drug.


Source: pSivida Corp.

However, in December 2013, the U.S. FDA threw a life-line to Alimera and partner pSivida by entering into an agreement to cancel a planned January 2014 Dermatologic and Ophthalmic Advisory Committee meeting in return for labeling discussions on the drug. As of the last update, Alimera will focus instead on drafting its response to the Complete Response Letter (CRL) received from the FDA in October 2013, with a goal of submitting the response in the first quarter of 2014.

According to Alimera, the response intends to address concerns the FDA raised regarding the facility at which Iluvien™ is manufactured. In addition, Alimera expects to provide a safety update and additional data on the product from patients and from physician experience with the applicator in the U.K. and Germany, where Iluvien is currently commercially available. The FDA has indicated that Alimera will not be required to conduct any new clinical trials in connection with the FDA's review prior to approval.



Source: pSivida Corp

Clinical data on Iluvien™ was recently published in the February 2013 issue of Drug (Vol. 73, Issue 2, 187-93). Results from two multinational trials in patients with DME previously treated with macular laser photocoagulation, fluocinolone acetonide intravitreal implant 0.2 µg/day was significantly more efficacious than sham injection in improving visual acuity. At 24 months post injection, 29% of fluocinolone acetonide intravitreal implant 0.2 µg/day recipients had an improvement in the best-corrected visual acuity (BCVA) letter score of ≥15 compared with 16% in the sham injection group (p=0.002).

Treatment benefit was most evident in the subgroup of patients whose duration of DME was ≥3 years. In this subgroup at 36 months, 34% of fluocinolone acetonide intravitreal implant 0.2 µg/day recipients had an increase in the BCVA score of ≥15, compared with 13% of sham injection recipients (p<0.001).

Iluvien™ looks like a far less effective drug than Eylea® (discussed below). Iluvien™ achieved a "percent of patients achieving a BCVA ≥15 letter score" of 29% at the end of two years compared to Eylea that seems to achieve 56-60% at the end of only 24 weeks. The benefits of Iluvien™ are the one-time injection that last up to three years. For a three year treatment with Eylea®, a DME patient might expect 22-36 injections.

However, high incidence of intraocular pressure (IOP, >21 mmHg) may limit Iluvien™ uptake. For example, the products UK prescribing label notes the proportion of Iluvien™ treated subjects requiring treatment with IOP lowering medication was 38% compared to 14% in the sham treated group. This proportion increased to 47% in those subjects with greater than median IOP at baseline (≥15 mmHg). Surgical interventions for the treatment of ocular hypertension were required in 4.8% of subjects treated with Iluvien™ compared to 0.5% of subjects treated with sham. Patients with high baseline IOP must be closely monitored when using Iluvien™. Besides high IOP, results from the FAME study show incidence of cataract surgery among all patients was approximately 3-fold higher for the Iluvien® group (80.0%) than in the sham group (27.3%).

With Lucentis® and Eylea® doing an estimated $1.3 billion and $650 million worldwide in DME, with about half the sales coming from the U.S., Iluvien™ looks like a $200 million U.S. and $100 million Ex-U.S. drug. Nevertheless, the Iluvien™ data and tenuous path to market in the U.S. represents an interesting benchmark for the development of a new treatment for DME.

VEGF-Inhibitors: Use of VEGF inhibitors have gained significant steam over the past decade since the approval of Genentech's Lucentis (ranibizumab) for age-related macular degeneration in June 2006, and the subsequent off-label use of Genentech's oncology drug, Avastin® (bevacizumab), a far cheaper and similar efficacy alternative. The properties of VEGF, and the consequences of its inhibition, also suggest a role for this approach in the management of DME. The mechanism of action for Lucentis® and Avastin®, inhibition of VEGF and other insulin-like growth factors that mediate angiogenesis, protease production, endothelial cell proliferation, migration, and tube formation is of similar concept in both oncology and ophthalmology indications. VEGF increases vascular permeability by relaxing endothelial cell junctions, which increases permeability and leakage. Inhibition of VEGF blocks this effect to some extent, as demonstrated in several recent clinical trials and case series involving the anti-VEGF molecules pegaptanib, ranibizumab, and bevacizumab.

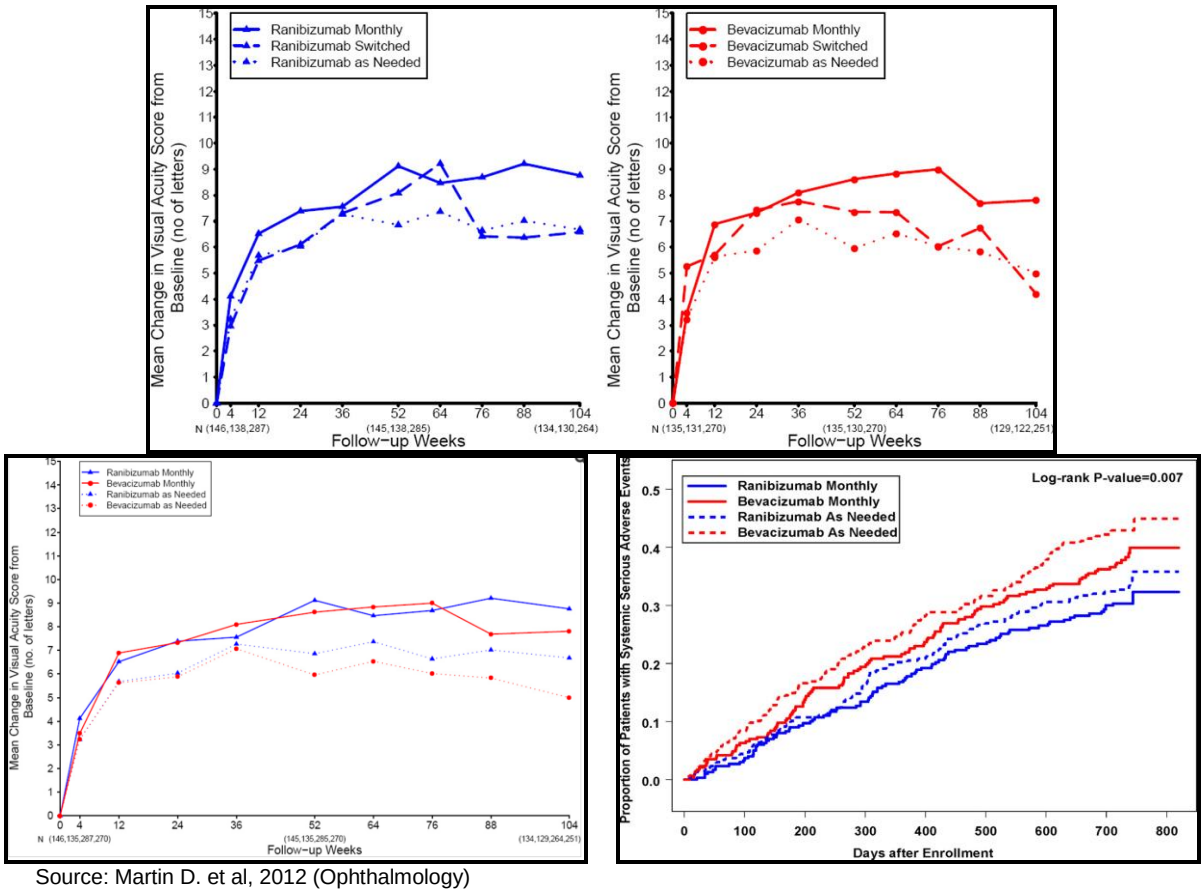
- ✓ Pegaptanib sodium (Macugen®, Valent Pharma) is an anti-VEGF aptamer, a small piece of RNA that self-folds into a shape that binds to and blocks the effects of VEGF165, one isoform of the VEGF family of molecules. The drug is approved by the FDA for the treatment of age-related macular degeneration. Results from a mid-stage DME study demonstrate that a modest mean improvement in baseline visual acuity in the pegaptanib 0.3-mg group versus a control. We regard the result as unimpressive.

- ✓ Ranibizumab (Lucentis®, Genentech) is an antibody fragment that also binds and blocks the effects of VEGF. Unlike pegaptanib, ranibizumab binds and inhibits all isoforms of VEGF. Lucentis® is approved by the FDA for the treatment of age-related macular degeneration and diabetic macular edema. We discuss the efficacy of ranibizumab below.

- ✓ Bevacizumab (Avastin®, Genentech) is the full antibody from which ranibizumab is derived. This anti-VEGF molecule is FDA approved for systemic treatment of metastatic colon cancer, but not for any ophthalmic indications. Its use in conditions such as age-related macular degeneration, diabetic retinopathy, and DME is currently off-label. The efficacy of Avastin® in AMD is comparable to that of Lucentis®. We discuss this below.

Avastin® vs. Lucentis®: Randomized clinical trials have been conducted comparing bevacizumab to ranibizumab for neovascular age-related macular degeneration. Results have been published in the New England Journal of Medicine (May 2011) and the Journal of Ophthalmology (July 2012). A total of 1,185 patients with neovascular age-related macular degeneration were enrolled in the clinical trial. A total of 1,107 of the 1,185 were followed for two years. At enrollment, patients were assigned to 4 treatment groups defined by drug (ranibizumab or bevacizumab) and dosing regimen (monthly or as needed). At 1 year, patients initially assigned to monthly treatment were reassigned randomly to monthly or as-needed treatment, without changing the drug assignment.

According to published results, among patients following the same regimen for 2 years, mean gain in visual acuity was similar for both drugs (bevacizumab-ranibizumab difference, -1.4 letters; 95% confidence interval [CI], -3.7 to 0.8; p=0.21). Mean gain was greater for monthly than for as-needed treatment (difference, -2.4 letters; 95% CI, -4.8 to -0.1; p=0.046). The proportion without fluid ranged from 13.9% in the bevacizumab-as-needed group to 45.5% in the ranibizumab monthly group (drug, p=0.0003; regimen, p<0.0001). Switching from monthly to as-needed treatment resulted in greater mean decrease in vision during year 2 (-2.2 letters; p=0.03) and a lower proportion without fluid (-19%; p=0.0001). Rates of death and arteriothrombotic events were similar for both drugs (p=0.60). The proportion of patients with 1 or more systemic serious adverse events was higher with bevacizumab than ranibizumab (39.9% vs. 31.7%; adjusted risk ratio, 1.30; 95% CI, 1.07-1.57; p=0.009). Most of the excess events have not been associated previously with systemic therapy targeting vascular endothelial growth factor (VEGF).



Source: Martin D. et al, 2012 (Ophthalmology)

Ranibizumab and bevacizumab had similar effects on visual acuity over a 2-year period. Treatment as needed resulted in less gain in visual acuity, whether instituted at enrollment or after 1 year of monthly treatment. There were no differences between drugs in rates of death or arteriothrombotic events. The interpretation of the persistence of higher rates of serious adverse events with bevacizumab is uncertain because of the lack of specificity to conditions associated with inhibition of VEGF. The primary impetus for significant off-label use of bevacizumab is cost. According to Ron Afashari, MD of the Yale School of Medicine and Director of the Yale Retina Service, Avastin® (bevacizumab) costs around $30 to $50 per dose when used off-label, whereas Lucentis® (ranibizumab) costs around $2,000 per dose. Roche sold an estimated $4.0 billion worth of Lucentis® in 2012. We estimate that approximately 1/3rd of the Lucentis® sales are off-label in DME.

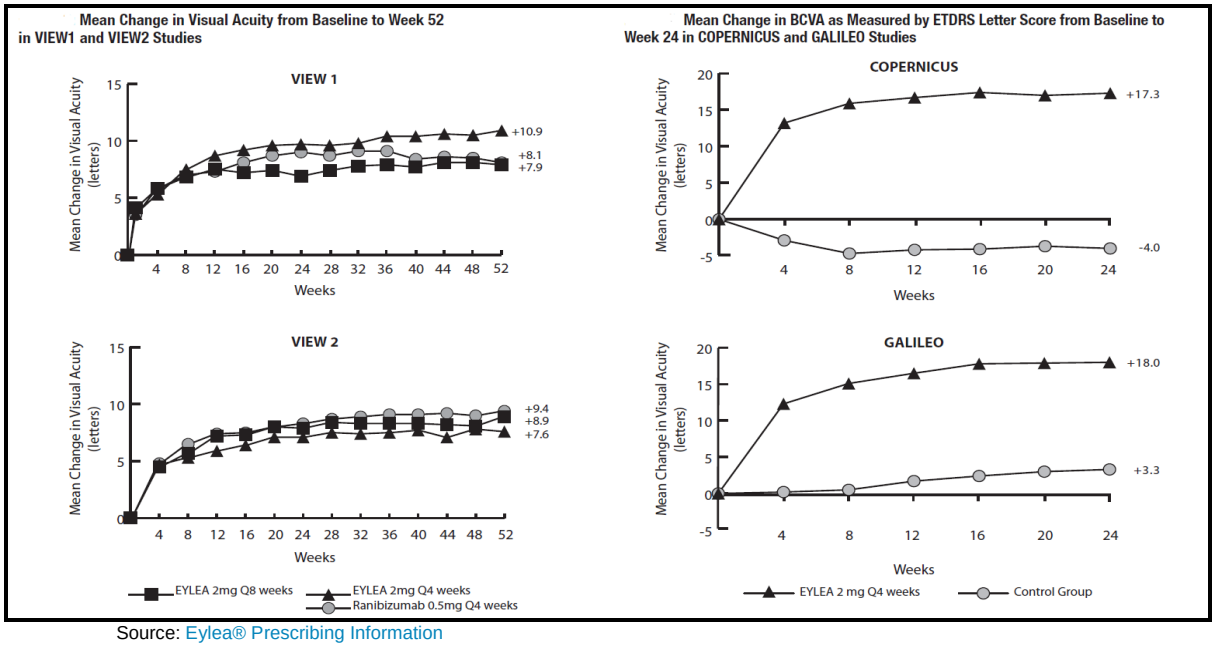
Aflibercept (Eylea®, Regeneron Pharmaceuticals) injection is a relatively new product for the treatment of (wet) age-related macular degeneration in November 2011. Since its approval, Eylea has gained significant market share on Lucentis® and Avastin® for AMD and off-label use in DME, primarily because the drug can be given every 4 weeks as oppose to the weekly injections with the aforementioned two. In fact, after the first 12 weeks of treatment, dosing can be titrated down to every 8 weeks. The drug is also approved for use in the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for five weeks, then every 8 weeks as a maintenance therapy. Elyea® 2013 worldwide sales are estimated at approximately $1.8 billion, with $1.4 billion in the U.S.

To gain approval, Regeneron conducted two Phase 3 studies in AMD, VIEW-1 and VIEW-2, and two additional Phase 3 studies, COPERNICUS and GALILEO in macular edema following CRVO. The data below highlights the primary efficacy findings for Elyea in both AMD and MD-CRVO:

Eylea®	AMD Studies				MD-CRVO Studies			
	VIEW-1		VIEW-2		COPERNICUS		GALILEO	
	Eylea 2 mg Q4	Lucentis 0.5 mg Q4	Eylea 2 mg Q4	Lucentis 0.5 mg Q4	Eylea 2 mg Q4	Control	Eylea 2 mg Q4	Control
Full Set Analysis	N=304	N=304	N=309	N=291	N=114	N=73	N=103	N=68
% of patients who maintained visual acuity (<15 letters BCVA loss)	95%	94%	95%	95%	56%	12%	60%	22%
Mean change in BCVA as measured by ETDRS letter score	+10.9	+8.1	+7.6	+9.4	+17.3	-4.0	+18.0	+3.3
% of patients who gained ≥15 letters of vision from baseline	38%	31%	29%	34%	-	-	-	-

Q4 = Dosing every 4 weeks, BCVA = Best Correct Visual Acuity
ETDRS = Early Treatment Diabetic Retinopathy Study, Time = 52 wks for AMD, 24 wks for DME

Source: Elyea® Prescribing Information



Source: Eylea® Prescribing Information

Regeneron just recently reported results from the 100 week follow-up analysis from the Phase 3 VISTA trial studying Eylea® for DME. In this trial, patients with DME were randomized to receive either Eylea® monthly (2Q4: n=155), Eylea® monthly for five months, then every two months as a maintenance (2Q8: n=152), or the comparator treatment of laser photocoagulation (n=154). Results showed a sustained improvement from baseline in best corrected visual acuity (BCVA) at week 100, compared to laser photocoagulation. The data at 52-weeks was previously reported, and included below.

Eylea®	Phase 3 VISTA Study					
	Eylea® 2 mg Q4		Eylea® 2 mg Q4 >> Q8		Photocoagulation	
	N=155		N=152		N=154	
TIME	1 Year	2 Years	1 Year	2 Years	1 Year	2 Years
Mean change from baseline BCVA	**12.5**	**11.5**	**10.7**	**11.1**	**0.2**	**0.9**
Safety Analysis						
Arterial Thromboembolic Events (% of patients)	**8.4%**		**7.2%**		**5.8%**	
All-Cause Mortality	**5.2%**		**2.6%**		**1.9%**	

We see the results from the VISTA study as particularly encouraging given that 43% of patients in this study had previously received anti-VEGF therapy. Besides demonstrating impressive improvement in BCVA after 100 weeks of treatment, Eylea® was generally well tolerated with a similar overall incidence of adverse events (AEs), ocular serious AEs, and non-ocular serious AEs across similar between the three cohorts. AEs were typical of those seen in other studies in patients with diabetes receiving intravitreal anti-VEGF therapy. The most frequent ocular AEs observed in the VISTA-DME trial included conjunctival hemorrhage, eye pain, and vitreous floaters. The most frequent non-ocular AEs included hypertension, anemia, and urinary tract infection. Overall the data for Eylea® compares well with Lucentis®. Adverse events for the two drugs are pretty similar, with conjunctival hemorrhage (25% vs. 28%), eye pain (9% for both), cataract (7% for both), and vitreous detachment and floaters (6-7% for both) the most common in the AMD studies. Eye pain (13% vs. 5%), conjunctival hemorrhage (12% vs. 11%), and intraocular pressure (8% vs. 6%) were the most common in the MD-CRVO studies.

Regeneron plans to present full two-year data from the VISTA-DME trial at upcoming medical conferences. Two-year data from the similarly designed VIVID-DME trial are expected later in 2014. Both the VISTA-DME and the VIVID-DME trials will continue as planned up to 148 weeks. Regeneron has filed regulatory submissions in the U.S. and the EU for Eylea® for the treatment of Diabetic Macular Edema.

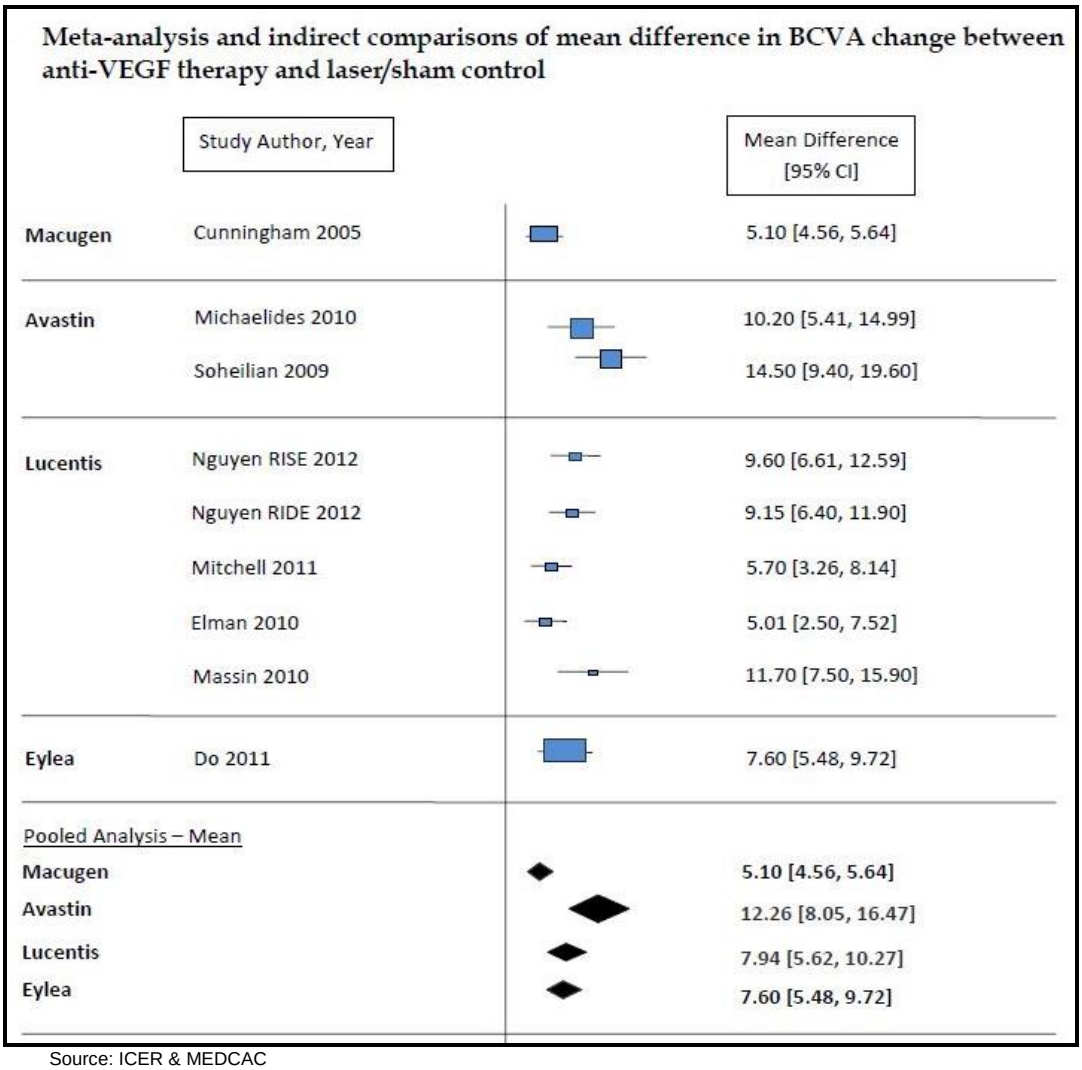
…Best Available Care – Based On Data & Cost…

In December 2013, a detailed paper was published in Therapeutic Advances in Endocrinology and Metabolism by Boyer D.S, et al (Vol. 4(6): 151-169) highlighting the data from all completed randomized Phase 2 or Phase 3 clinical trials with anti-VEGF therapy in patients with DME. The authors conclude:

> *The previous standard of care for patients with DME has focused on the prevention of further deterioration in vision using **macular laser** once some degree of loss has already occurred, with **very few patients experiencing any subsequent gains in vision**. Studies of the pathophysiology of DME demonstrate a **crucial role for VEGF in disease development** and this has led to successful clinical trials of VEGF inhibitors. Data from several large, prospective randomized clinical trials indicate that, on average, **intraocular inhibition of VEGF is associated with rapid resolution of DME** (as indicated by reduction of the thickness of the retina) and significant VA gains, **better than those achieved with focal/grid laser photocoagulation**, demonstrating that the focus of treatment should be on improvements in vision and not the prevention of further worsening.*

In May 2012, the Institute for Clinical and Economic Review (ICER) prepared a technology assessment report on anti-vascular endothelial growth factor treatment for diabetic macular edema. The report was prepared for the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC). ICER analyzed a total of 15 randomized clinical trials and eight observational studies. The authors of the report concluded that anti-VEGF therapy improves visual acuity in patients with DME relative to macular laser treatment of sham injection. However, no significant difference between the anti-VEGF agents was found in terms of clinical performance, and the authors cautioned that the unknown systemic side-effect profile of drugs like Avastin® relative to Lucentis® and Eylea® remains the greatest element of uncertainty.

Below is a figure from the report highlighting the prospective efficacy findings from “fair” or “good” quality studies with anti-VEGF therapy.



Source: ICER & MEDCAC

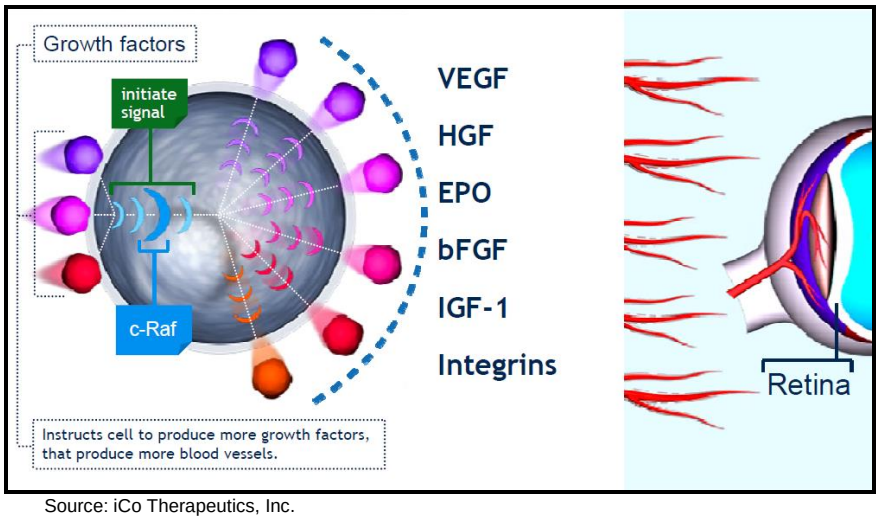
Based on the results of the head-to-head analysis conducted by Martin D. et al, 2012 (Ophthalmology) and the technology assessment report prepared by ICER for MEDCAC, off-label use of Avastin® (bevacizumab) seems like the most effective anti-VEGF therapy for DME. Efficacy results look similar to Lucentis® (ranibizumab), with cost for yearly treatment favoring the off-label bevacizumab by nearly 40-to-1. We estimate one year treatment of Lucentis® (at approximately $2,000 per dose) costs $18,000 to $24,000, whereas yearly treatment with off-label use of bevacizumab (currently priced at around $50 per dose) costs only $450 - $600.

Regardless of the efficacy and economics that seem to favor off-label use of Avastin®, Lucentis® and Eylea® are generating over $3.3 billion in sales in DME. The systemic side-effect profile of Avastin® and the lack of physician desire to dilute out off-label bevacizumab, as well as aggressive marketing by Roche, is what are driving use of Lucentis®. We believe use of Eylea®, priced at roughly a 5% discount to Lucentis®, is being driven by less frequent dosing after the initial 24 week treatment phase. Regeneron Pharma has aggressively marketed Eylea® as “lasting longer” than Lucentis®, thus requiring fewer injections per year. Although the actual number of injections only marginally favors Eylea® at roughly 8-9 per eye per year vs. Lucentis® at 10-12 per eye per year, the advantage has been enough – with similar efficacy – to generate over $2.0 billion in sales in AMD and DME, combined.

Therefore, **WE CONCLUDE** that a significant market opportunity exists for a product with equal efficacy to the anti-VEGF therapies, assuming there are improvements in both systemic safety and dosing frequency.

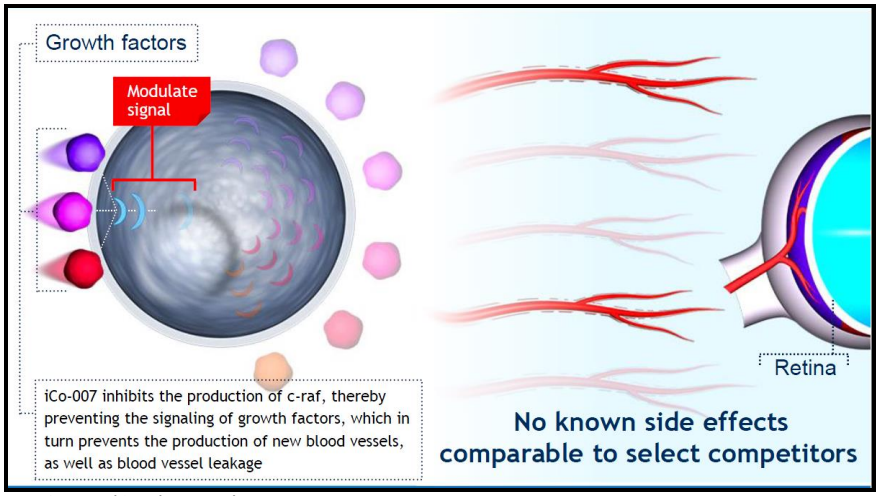
Enter iCo Therapeutics – iCo-007

Vancouver, Canada based iCo Therapeutics is developing iCo-007, a second generation antisense drug in-licensed from ISIS Pharmaceuticals in 2005 for the treatment of diabetic macular edema. iCo-007 is designed to block c-Raf (also known as Raf-1), a protein kinase involved in transmitting the signal generated when VEGF and other growth factors believed to be important in DME bind to their cell surface receptors. This binding initiates a signaling cascade response resulting in aberrant cell growth and/or angiogenesis. The raf gene family includes three highly conserved genes termed A-raf, B-raf and c-raf. Raf genes encode protein kinases that play important regulatory roles in signal transduction processes that regulate cell proliferation and angiogenesis (US 20130028889). Research shows that aberrant cell growth and/or angiogenesis has been associated with a variety of ocular diseases and disorders, including, but not limited to, macular edema, macular degeneration, diabetic retinopathy, and retinopathy of prematurity. By targeting c-raf, the antisense oligonucleotide, iCo-007, is designed to inhibit raf gene expression and cell growth, leading to reduced ocular neovascularization.

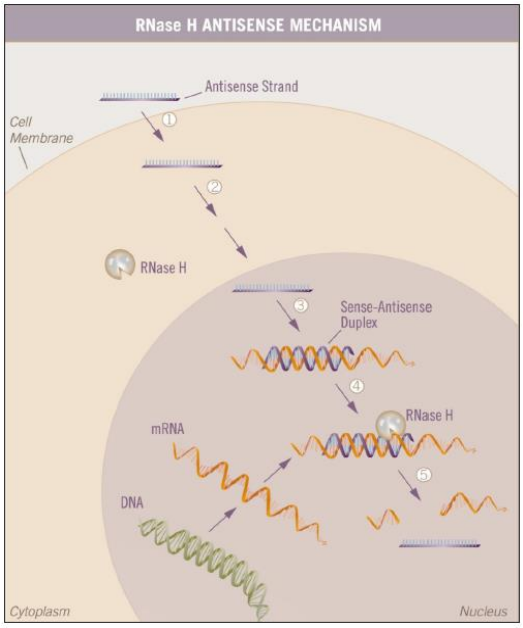


Source: iCo Therapeutics, Inc.

By blocking multiple pathways involved in the pathogenesis of DME, iCo-007 could potentially provide greater efficacy than VEGF blockers such as Lucentis® and Eylea®. Work done by Mohammad G. et al, 2011 and published in the April 2011 (Vol 15(4): 357-364) issue of Expert Opinion Therapeutic Targets qualifies the role of Raf-mediated signaling pathways as they relate to diabetic retinopathy. The authors conclude that Raf kinase is involved in a variety of functions, including the cell cycle, proliferation and apoptosis. In animal models of diabetic retinopathy, Raf kinase is activated in the retina and its microvasculature. Activated Raf kinase is associated with increased apoptosis of retinal capillary cells, the process that precedes the development of retinal histopathology, and inhibition of Raf kinase ameliorates apoptosis.



Source: iCo Therapeutics, Inc.



Source: Hnik P. et al, 2009

In July 2009, Hnik et al published a detailed analysis of the mechanism of action for iCo-007 in the Journal of Diabetes Science and Technology (Vol.3, Issue 4:924-931), titled *Antisense Oligonucleotide Therapy in Diabetic Retinopathy*. The authors conclude that a number of growth factors critical for neo-vascularization and leakage signal through the MAP kinase cascade, which includes c-Raf kinase, and are involved in cellular processes regulating proliferation, differentiation, and apoptosis. Other growth factors, such as erythropoietin, hepatocyte growth factor, basic fibroblast growth factor, and others, may play important roles in the etiology of diabetic retinopathy and DME.

Inhibiting a downstream target such as c-Raf kinase may prove to be a more effective treatment strategy by down regulating multiple growth factors as opposed to targeting individual growth factors only. An antisense oligonucleotide, such as iCo-007, delivered via an intravitreous injection seems to be a reasonable strategy in the treatment of retinal diseases given that experimental treatments targeting VEGF have shown clinical efficacy, and down regulating multiple growth factors that seem to play a critical role in the process of ocular angiogenesis and leakage hold scientific merit.

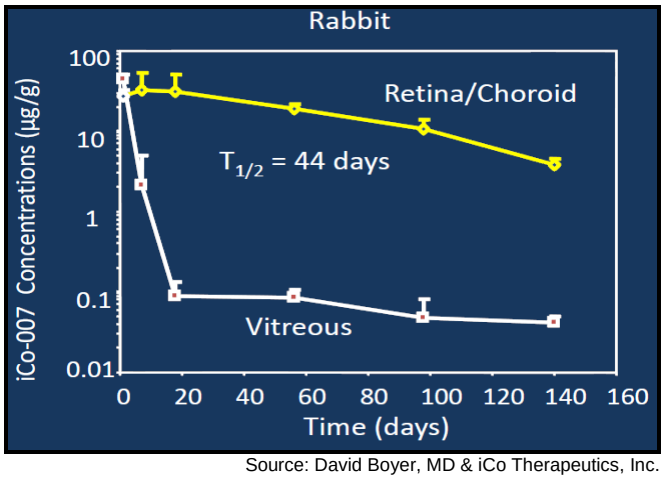
Hnik P. et al conclude that iCo-007 may result in a more potent anatomical effect (retinal thickness), as well as a functional effect (vision) than current anti-VEGF therapy. The authors believe that the benefits of iCo-007 include an extended half-life, resulting in less frequent intravitreal drug administration, resistance to molecule degradation, a good safety profile, and, due to a differing mechanism of action, the possibility of adjunct therapy to other agents or procedures.

Therefore, **WE CONCLUDE** based on a preponderance of evidence in the scientific literature (1, 2, 3, 4, 5) that the mechanism of action for iCo-007 has significant merit, and intravitreal injection of an antisense oligonucleotide is both clinically and commercially validated by the approval of Vitravene (6).

…iCo-007 Preclinical Data…

In preclinical rabbit and monkey studies, iCo-007 demonstrated an extended half-life (t½) in the retina between 6 and 8 weeks. The company has stated that it believes the results of these studies may support the potential of iCo-007 to be administered in humans at intervals of once every three to six months (source).

Tissue Concentration (µg/g)		
Dose (µg)	Single	Multiple x 3
90	32.2 ± 22	81 ± 37



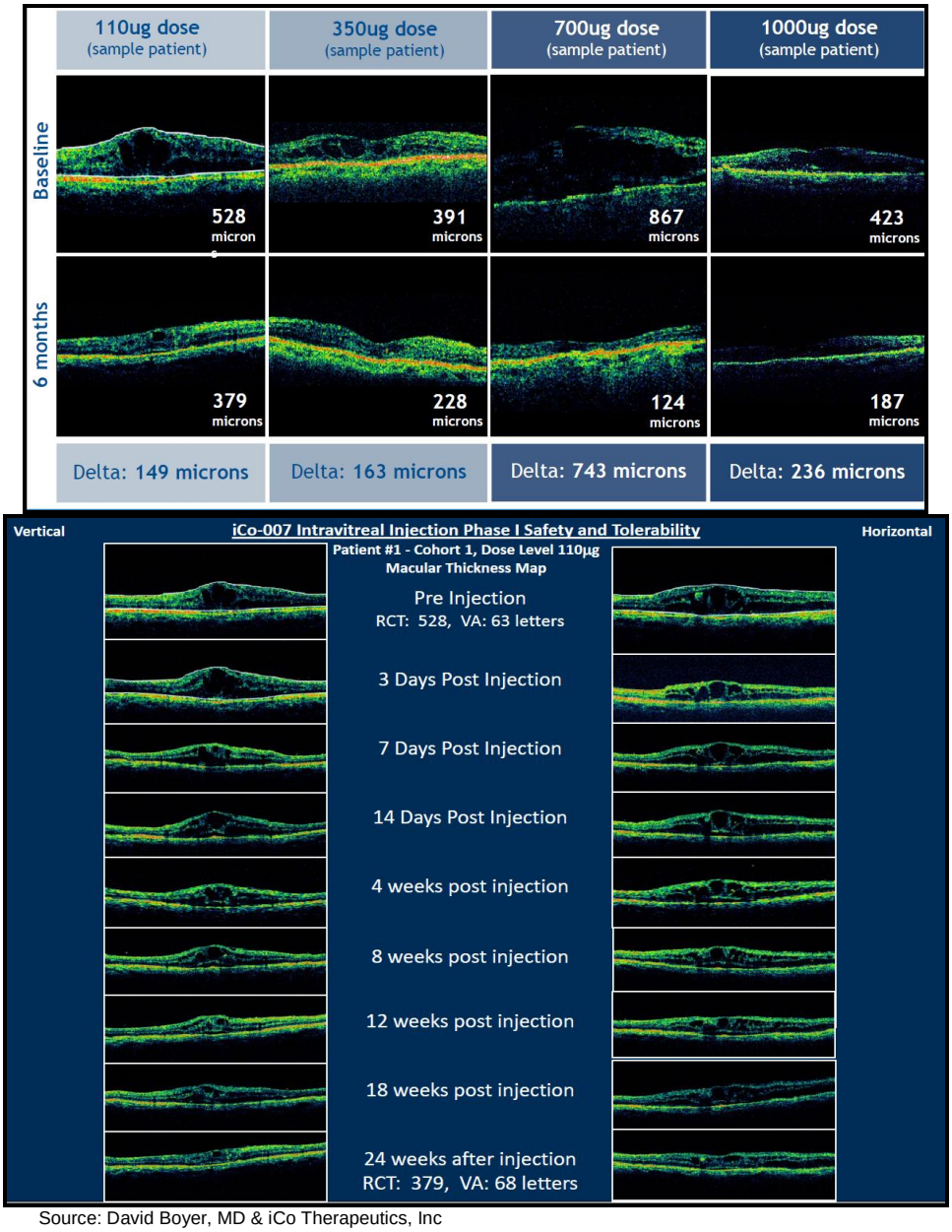
Source: David Boyer, MD & iCo Therapeutics, Inc.

Results of single and multiple dosing regimens show good tissue concentration and slow clearance from the retina. We believe this could be an important differentiator in the marketing of the drug given intravitreal injection remains a source of anxiety for patients with eye disease.

…iCo-007 Phase 1 Data…

In May 2010, iCo Therapeutics announced results from an open-label Phase 1 clinical trial examining the safety and efficacy of 110 ug, 350 ug, 700 ug, or 1000 ug of iCo-007 administered via single intravitreal injection in 15 patients with diffuse macular edema. Diffuse DME is considered more difficult to treat than focal DME, which involves a smaller portion of the retina. All of these patients were non-responders to previous therapies, including photocoagulation, steroids, and anti-VEGF therapeutics such as Avastin® and Lucentis®. All patients had either Type-1 or Type-2 diabetes, with BCVA at baseline of 60-15 letters (ETDRS) or approximately 20/63 to 20/500 (Snellen). Visits took place at Day 0, Day 3, Day 7, Week 2, Week 4, Week 8, Week 12, Week 18 and Week 24. At all visits, patients were evaluated for changes in central retinal thickness (a measure of edema) and visual acuity. Among the 12 patients available for evaluation at 24 weeks (5.6 months), changes in retinal thickness in responsive patients were -149 to -743 uM, with a mean value of -169 uM. Data from the Eylea® COPERNICUS study, 2 mg every four weeks resulted in range of -127 to -195 uM reduction in central retinal thickness after 24 weeks after six injections (source: Brown DM, et al, 2013).

Optical coherence tomography images for some of these patients are presented below. These show continuing improvements in macular edema between Weeks 18 and 24 of the study, supporting the potential for an extended period between injections.



Source: David Boyer, MD & iCo Therapeutics, Inc

Thirteen patients were available for evaluation of visual acuity at the end of the 24-week treatment period; 9 of these had stable or improved vision (defined as a -5 letters BCVA or better compared to baseline) and three had a 5-letter or greater increase relative to baseline. From a safety standpoint, we note iCo-007 was not detectable in blood plasma, as expected from the low dose and its local administration into the eye. Additionally, there were no drug-related SAEs as assessed by the investigator.

We believe the efficacy results for this trial compare very well to Lucentis®, Elyea®, and Iluvien®. It is difficult to draw a firm comparison between iCo-007 and the other agents because of the different interval between treatment and efficacy evaluation, and the lack of a disclosed mean change in visual acuity. However, the overall effect on macular thickness for iCo-007 looks impressive. That being said, the effect on visual acuity appears smaller than many of the other agents. However, we emphasize that this is a comparison of treatment effects seen six months after a single injection of iCo-007 to those seen after a 6 month, multi-injection treatment regimen of the other agents (many patients had end-stage disease).

The data is at least compatible with the hypothesis that iCo-007 can provide results comparable to those obtained with Lucentis® and Elyea®, but with a longer interval between injections. In our view, this represents an important commercial advantage. For example, Iluvien® allows very long intervals between injections, but is saddled with steroid side effects including a clinically significant increase in ocular pressure (which predisposes to glaucoma) and cataracts, and analysts that cover Alimera Sciences have estimated Iluvien® at $200 million in U.S. sales (source: Zacks Consensus).

…The Phase 2 iDEAL Study…

In March 2012, iCo Therapeutics initiated enrollment in iDEAL (NCT01565148), a Phase 2 study designed to explore whether varying combinations and concentrations of iCo-007 are effective in improving visual acuity in people with diabetic macular edema. The trial is co-sponsored by the Juvenile Diabetes Research Foundation (JDRF), which provides certain negotiated cost discounts and improved pricing metrics for iCo Therapeutics. For instance, we believe the cost of iDEAL to iCo Therapeutics is around $6 million, whereas without JDRF support the trial might have costs upward of $10 million.

To be eligible for the trial, participants must have Type-1 or Type-2 diabetes, baseline best corrected visual acuity between 20/32 and 20/320 and DME with central retinal thickness equal to or greater than 250 microns measured by optical coherence tomography (OCT). In iDEAL, patients will receive repeated intravitreal injections of iCo-007 as a monotherapy and in combination with ranibizumab (Lucentis®) or laser photocoagulation, randomized into one of four treatment groups noted below:

1. Intravitreal dosing of 350 µg iCo-007 at baseline and Month-4
2. Intravitreal dosing of 700 µg iCo-007 at baseline and Month-4
3. Intravitreal dosing of 350 µg iCo-007 at baseline + laser photocoagulation Day-7, then another intravitreal dosing of 350 µg iCo-007 at Month-4 + laser photocoagulation at seven days later (if necessary).
4. Intravitreal dosing of 0.5 mg ranibizumab (Lucentis®) at baseline + 350 µg iCo-007 at Day-14, then a repeat dose of 0.5 mg ranibizumab at Month-4 + 350 µg iCo-007 14 days later.

The primary endpoint of the iDEAL study is mean change in visual acuity (VA) from baseline to month eight. Primary safety outcome measures include the number of participants in a given study arm experiencing the same drug-related serious adverse event as a measure of safety and tolerability at month 12 and safety of repeated iCo-007 intravitreal injections in treatment of subjects with DME as monotherapy and in combination with ranibizumab or laser photocoagulation throughout the entire study. Secondary outcome measures include change in VA from baseline to month 12, change in retinal thickness measured by OCT from baseline to month eight and 12, duration of iCo-007 treatment effect during the 12 month follow-up period as measured by VA and OCT thickness, and then peak plasma concentration (C_{MAX}) of iCo-007 after multiple injections.

The mid-point of the trial was reached in January 2013, and the company announced no serious drug-related adverse events among patients receiving repeat doses of iCo-007. In June 2013, the company announced that enrollment was completed at 187 patients (randomized). Recruitment took place at roughly 28 clinical sites across the United States. The iDEAL study is a multi-center study chaired by Quan Dong Nguyen, MD, MSc, Professor and Chair of Ophthalmology and Director of the Stanley M. Truhlsen Eye Institute at University of Nebraska Medical Center (UNMC). In addition, the Retinal Imaging Research and Reading Center (RIRRC) based at the UNMC serves as the Reading Center for the iDEAL Study.

We are expecting top-line results from the iDEAL study in April 2014. This data will include the initial analysis of the primary endpoint at month eight. The trial is scheduled to continue to month twelve, where a full analysis of the primary endpoint at month eight will be complimented by additional analysis at month twelve and a full safety set analysis of all patients receiving iCo-007, laser photocoagulation, and Lucentis®. We expect this data around the September / October timeframe.

…What's Next…

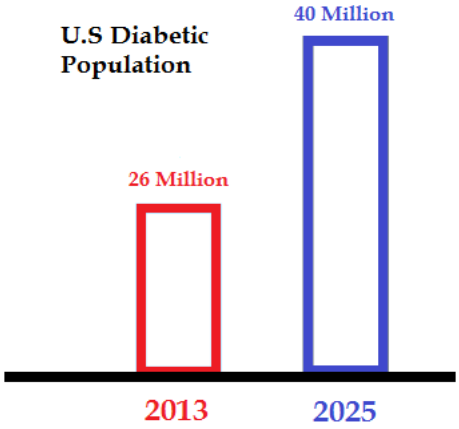
Results from the iDEAL study should help management plan the next stage in development for iCo-007. The results from the Eylea® VISTA-DME study have set the bar high. However, the potential for less frequent dosing (quarterly vs. monthly or every other month) present a very interesting market share grabbing opportunity if iCo-007 can demonstrate 10-12 lines of improvement on BCVA similar to Eylea®. However, other interesting development pathways exist for iCo Therapeutics should the results fall shy of Eylea's impressive data from VISTA. Specifically, results in anti-VEGF non-responders will be very important for the future development of the drug. Data shows that approximately 30-40% of DME (and AMD) patients are non-responders to drugs like Lucentis® and Eylea® (7, 8).

For iCo Therapeutics, the pending results of the iDEAL study represent a major potential inflection point in the company's valuation. If results from iDEAL are positive, iCo is sitting on a potential blockbuster drug. The trajectory for U.S. sales of Eylea® (consensus for 2014 sales is $1.8 billion) has been extremely impressive given the only modest improvement in efficacy over Lucentis® and Avastin®. Uptake is being driven by improvements in dosing and safety. The potential profile for iCo-007 offers further improvements in both over Eylea®. It comes down to whether or not the iDEAL study offers the data on the efficacy side to validate the thesis.

The next steps after the full iDEAL data in September / October 2014 are to schedule a meeting with the U.S. FDA to go over the results and outline the protocol for the Phase 3 studies. As noted above, it's a little early to predict what the potential Phase 3 studies will look like until we see the data from iDEAL. iCo Therapeutics could be looking at a broad monotherapy superiority or non-inferiority study to Lucentis®, or a combination therapy trial with anti-VEGF, or a smaller program in anti-VEGF non-responders.

…Market Opportunity For iCo-007…

According to the American Diabetes Association, 25.8 million Americans have diabetes. However, according to the National Diabetes Education Program, as many as 79 million are pre-diabetic. By 2025, the ADA expects over 40 million American's to have diabetes. The primary risk factor for DME is dyslipidemia. Above we noted a prevalence study suggesting approximately 1.8 million people in the U.S. with DME. Data suggest the population with diabetic retinopathy is as much as 4-times the size of the DME population.



Sales of Lucentis®, primarily indicated for age-related macular degeneration, totaled roughly $4.0 billion in 2013. Analysts that cover Roche estimate approximately 2/3^{rds} of the sales are in AMD, with the remaining 1/3rd in DME. For Regeneron's Eylea®, sales in 2013 were $1.8 billion, of which roughly 1/3rd is in DME. We estimate the total size of the DME market at roughly $5.0 billion.

As noted above, the driving factors for use of anti-VEGF therapies are: 1) superior efficacy vs. macular laser or corticosteroid injection, 2) ability to restore or improve vision loss, 3) less frequent dosing, 4) system safety and tolerability, and 5) cost. It is difficult to forecast sales of iCo-007 prior to the presentation and our analysis of the Phase 2 data from iDEAL. Following the results of iDEAL, we believe iCo Therapeutics would like to move quickly into partnership discussions with on a regional basis for the pivotal registration trials and commercial sales of the product post approval.

What seems clear to us is that with similar efficacy comparable to drugs like Lucentis® and Eylea®, along with better systemic safety and the potential for less frequent dosing, iCo-007 could be a $1.0 billion drug in DME. As a combination therapy or with a label for anti-VEGF non-responders, iCo-007 is still a $500 million drug.

Intellectual Property

The composition of matter patents on iCo-007 expire in 2014-2016, which is clearly before the compound can be brought to market given its current stage of development. Other protection is provided by the ISIS patents on second-generation antisense technology, which has been licensed exclusively to iCo Therapeutics. Specifically, intellectual property rights for iCo-007 are protected in that under the licensing agreement with iCo, ISIS will not develop or commercialize or grant any sub-license or other rights to a third party to develop or commercialize any antisense RNA or analog thereof that directly inhibits C-Raf kinase (the target for iCo-007) expression or translation. These process chemistry patents are expected to run to 2023 or later, but this is still only 5 years after the expected approval date of iCo-007, and these patents would presumably not be eligible for patent term extension under the Hatch-Waxman amendment.

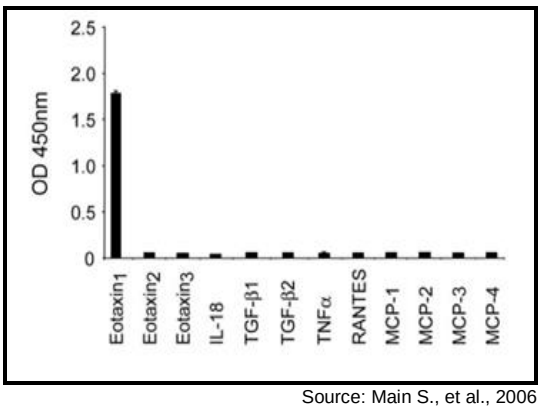
The company reports that it has applied for additional patents to protect iCo-007. One such patent has published on the USPTO website (the usual delay after filing being 18 months). Application 13/577,219 claims a method of treating macular edema, comprising administering an anti-c-Raf oligonucleotide no more frequently than once every 90 days. Given the novelty and utility of such infrequent administration, we believe there is at least a 50% chance that this application could be granted and successfully defended in court. We expect, however, that it will be a few years until a final decision is available from the USPTO, as the application was only just filed in 2011. If granted and successfully defended, protection would be available for 15 years or more post-approval.

For purposes of our valuation, we assume that the exclusivity on iCo-007 will be limited to the data exclusivity provided by the Hatch-Waxman Act. The terms of the Act forbid the filing of an NDA on a new chemical entity for 5 years post-approval. This 5 years can be extend by 6 months for performing pediatric studies. Adding to this the approximately 2 years required by the FDA to process a typical ANDA application, we estimate the marketing exclusivity available to iCo on iCo-007 will be around 7 to 8 years post approval.

Multiple Shots On Goal With iCo-008

In January 2007, iCo Therapeutics entered into a worldwide licensing transaction with Cambridge Antibody Technology (CAT) for the exclusive development and commercialization rights to CAT's bertilimumab (CAT-213), a first-in-class fully human IgG4 monoclonal antibody discovered using CAT's phage display technology. Under the terms of the deal, iCo will have sole responsibility for all future clinical development and commercialization of the antibody in return for paying CAT, later acquired by AstraZeneca Corp., a $400,000 upfront fee, along with up to $7.0 million in clinical and regulatory ophthalmology-related milestone payments, plus royalties on future product sales. Richard Mason, CAT's SVP Business and Commercial Operations commented at the time that "Following an internal review of our development priorities, CAT decided to out-license CAT-213." iCo stated that they planned to advance CAT-213 initially for the treatment of ocular allergies including allergic conjunctivitis.

Bertilimumab, now dubbed iCo-008, is a first-in-class fully human IgG4 monoclonal antibody targeted against eotaxin-1. The antibody binds to eotaxin-1 with very high affinity (~80 pM) and a series of experiments conducted by Main S., et al published in Pharmacology and Experimental Therapeutics (Vol.319,No.3) validated its specificity and activity. Most importantly, ELISA analysis was conducted using a series of human cytokines and chemokines, including the functionally related eotaxin-2 and eotaxin-3 (see graph to the right). The high sensitivity of the ELISA coupled with the high antigen coating concentrations and the lack of any cross-reactivity indicates that bertilimumab is highly specific to eotaxin-1. This high degree of specificity and affinity should decrease any off-target effects or toxicities due to cross-reactivity with other antigens.



Source: Main S., et al., 2006

…Brief Clinical History Of Bertilimumab…

CAT conducted three separate clinical trials with bertilimumab in the early 2000's to determine the pharmacokinetics, safety and effectiveness in treating allergy, allergic rhinitis and conjunctivitis. We provide a brief history of these programs below:

- Phase 1: The pharmacokinetics of CAT-213 was assessed in an ascending single dose, single-blind Phase 1 study. Twenty-five healthy male volunteers were administered 0.01, 0.1, 1, 5 and 10 mg/kg intravenously over 30 min. Results show no serious adverse events reported and a half-life at the highest concentration of approximately 8.4 days.

- Phase 2: A double-blind, placebo controlled study was undertaken to assess the effect of CAT-213 on allergen-induced rhinitis through intravenous or intranasal dosage 30 minutes prior to exposure to an antigen. A total of 52 patients with history of seasonal allergies were entered into the study. The primary endpoint was the reduction in nasal cross-sectional area as assessed by acoustic rhinometry. The results showed that CAT-213 administered intranasally attenuated the post allergen nasal obstruction for up to six hours; however there was no demonstrated effect on either peak nasal inspiratory flow or symptoms. The infiltration and activation of cells from nasal lavage samples were collected pre-dosing and 30, 60, 120, 360 and 480 minutes after allergen challenge, and a nasal biopsy was performed six hours post challenge. The results of the lavage showed a trend for reduction in eosinophils following treatment with CAT-213, though this effect was not statistically significant. For the biopsy, submucosal mast cells were significantly decreased by intravenous and intranasal CAT-213 compared with placebo. Intranasal CAT-213 also significantly and notably decreased submucosal eosinophil infiltrate.

- Phase 1/2a: An allergen challenge study was carried out using a topically applied single dose of CAT-213 in patients with allergic conjunctivitis. CAT-213 did not have any effect on symptoms as analysis showed that allergen challenge did not provoke a large enough late-phase response involving eosinophils.

The early clinical trial results using CAT-213 were not particularly encouraging from an efficacy standpoint. However, while the total number of patients tested with the drug was limited (<150), CAT-213 was safe and well tolerated with no serious side effects reported. We believe that the lack of efficacy noted for CAT-213 is due to the fact that there was no selection for patients with increased eotaxin-1 levels, the patient population most likely to respond to bertilimumab in future studies.

Eotaxin, a chemo-attractant for eosinophils and a ligand for chemokine receptor 3 (CCR3), represents a well-established target for multiple allergic conditions. iCo-008's pre-clinical and clinical history indicates that iCo-008 may be effective in several large market systemic indications, including severe asthma, food allergies and allergic rhinitis. iCo's non-ophthalmic development partner, Immune Pharma, has teamed up with contract manufacturing organization, Lonza, to manufacture product for future clinical studies. Lonza is one of the world's leading suppliers to the pharmaceutical industry in the production of active pharmaceutical ingredients and has been manufacturing the product in its cGMP facilities in Slough, UK.

…Ocular Indications…

VKC → In March 2008, iCo announced that it planned to develop iCo-008 for Vernal Keratoconjunctivitis (VKC), recurrent, bilateral, chronic inflammation of the conjunctiva. VKC is most common in young boys between three to 16 years of age, though it may appear earlier than that and continue into adulthood. Symptoms include intense itching, irritation, photophobia (sensitivity to light) and burning. The itching is worse with exposure to wind, dust, bright light, and hot weather. Some patients complain of a sticky, stringy mucous discharge. In the majority of cases, symptoms are self-limiting and having a periodic seasonal incidence. In severe cases, corneal involvement leads to complaints of reduced vision and even vision loss. Signs of VKC can be described in three clinical forms:

- ✓ Palpebral form – Usually upper tarsal conjunctiva of both the eyes is involved. Typical lesion is characterized by the presence of hard, flat-topped papillae arranged in cobblestone or pavement stone fashion. In severe cases papillae undergo hypertrophy to produce cauliflower-like excrescences of giant papillae.
- ✓ Bulbar form – It is characterized by dusky red triangular congestion of bulbar conjunctiva in palpebral area, gelatinous thickened accumulation of tissue around limbus and presence of discrete whitish raised dots along the limbus (Tranta's spots).
- ✓ Mixed form – Shows the features of both palpebral and bulbar types.

Scientists believe VKC may have an IgE mediated mechanism. Patients often give family history of other atopic diseases such as hay fever, asthma or eczema, and their peripheral blood shows eosinophilia and increased serum IgE levels. The pro-inflammatory cytokine, eotaxin-1, plays an important role in mast cell degranulation and attracting eosinophils to inflammation sites – a condition called eosinophilia. Research done by Cambridge Antibody Technology shows bertilimumab is a potent inhibitor of eotaxin-1. The release of eotaxin-1 from these cells is thought to contribute to the local accumulation of eosinophils in inflammatory conditions (Gleich GJ, 2000).

Clinical and preclinical evidence proves that by blocking eotaxin-1 can result in effective inhibition of early phase mast cell activation as well as late phase eosinophilia. This broad-spectrum mechanism of action seems uniquely ideal for treating VKC. The relationship between this mechanism of action and allergic conjunctivitis was studied in a mouse model by Miyazaki D., et al, with results published in International Immunology in 2009 (Vol.21,No.2,187-201). The authors concluded that eotaxin-1 is a critical mediator for IgE mediated mast cell activation and provides the igniting signal for ocular allergic reactions.

Management is currently in discussion with potential partners on a Phase 2 study with iCo-008 in VKC to start later in 2014. Incidence of VKC is highest in Japan and around the Mediterranean Sea, most notably in Italy, Greece, Turkey, Israel, and northern Africa. We believe there is significant potential to find a partner for Japan (and additional Asian territories) or assist independent investigators in Italy with small pilot studies with a goal of showing proof-of-concept prior to entering into a larger development and commercialization deal perhaps in 2015.

AMD → Beyond VKC, iCo Therapeutics believes that iCo-008 may offer clinical utility in wet age related macular degeneration (AMD). AMD is a common eye condition and leading cause of vision loss among people age 50 and older. Development of AMD results in a loss of vision in the center of the visual field (the macula) because of damage to the retina. The disease occurs in "dry" and "wet" forms. In the dry (non-exudative) form, cellular debris called drusen accumulates between the retina and the choroid, and the retina can become detached. In the wet (exudative) form, which is more severe, blood vessels grow up from the choroid behind the retina.

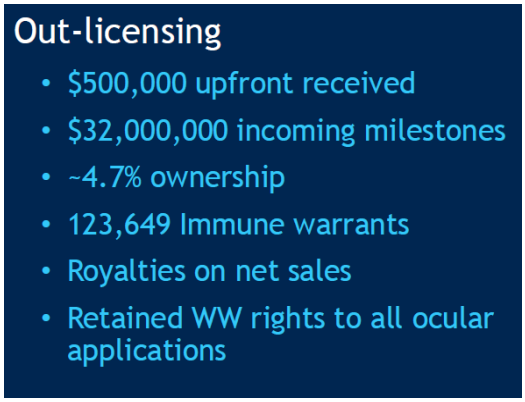
Similar to DME, It can be treated with laser coagulation, and with medication that stops and sometimes reverses the growth of blood vessels. The leading drug therapies to treat AMD are the anti-VEGF agents noted above, Lucentis®, Avastin®, and Eylea®, with Eylea® gaining significant share vs. Lucentis® on improved safety and less frequent dosing. We believe that Iluvien™ will capture only modest market share in AMD once approved in the U.S. given the risk of higher IOP and increased development of cataracts.

The primary mechanism of action for eotaxin-1 to signal cell response is through binding to Cys-Cys chemokine receptor 3 (CCR3). CCR3 is expressed on all cells such as eosinophils, basophils, mast cells, dendritic cells, and T-helper cells. On binding to the eosinophilic CCR3, eotaxin-1 causes intracellular calcium mobilization, initiation of intracellular actin polymerization, up-regulation of integrin expression and the induction of oxygen radical production (Ding C., et al, 2004). Results from the work done by Miyazaki D., et al, noted above shows that CCR3 blockade significantly suppresses allergen-mediated hypersensitivity reactions as well as IgE-mediated mast cell degranulation. The authors conclude that CCR3 has a pivotal role in activation of mature connective tissue-type mast cells in the ocular tissue (Takeda, A. et al, 2009).

A paper published by Takeda, A., et al and published in the June 2009 issue of Nature (Vol.460:225-230) shows that the eosinophil / mast cell chemokine receptor CCR3 is specifically expressed in choroidal neovascular endothelial cells in humans with AMD, and that despite the expression of its ligands eotaxin-1, -2 and -3, neither eosinophils nor mast cells are present in human choroidal neovascularisation (CNV). Results of this work show that genetic or pharmacological targeting of CCR3 or eotaxins inhibited injury-induced CNV in mice through direct inhibition of endothelial cell proliferation. CCR3 targeting might reduce vision loss due to AMD through early detection and herapeutic angio-inhibition. The authors conclude that CCR3 blockade was more effective at reducing CNV than vascular endothelial growth factor-A (VEGF-A) neutralization, as well as being less toxic in mouse models of the disease.

…Out-License To Immune Pharmaceuticals…

In December 2008, iCo Therapeutics granted Immune Pharmaceuticals an exclusive license option for the development and commercialization rights to bertilimumab for systemic uses. This included all rights outside of ocular indications. The option agreement came with a non-refundable $1 million option fee creditable upon conversion to an upfront payment if executed to a full licensing agreement. This agreement was fully executed in June 2011. In total, iCo Therapeutics could receive up to $32 million in milestones from the development of bertilimumab in systemic indications focused on irritable bowel disease. Immune is also pursuing a potential orphan disease indication in Bullous Pemphigoid (BP), an orphan autoimmune indication mediated blistering skin disease.



As part of terms of the deal, iCo therapeutics received 600,000 shares and warrants to purchase an additional 200,000 shares at $0.95 per share in Immune Pharmaceuticals (IMNP). As of the company's most recent investor presentation, iCo Therapeutics currently owns 654,486 shares and 123,649 warrants in Immune Pharma. The share ownership in Immune amounts to roughly $2.3 million in value.

Immune has initiated two Phase 2 trials to test bertilimumab in both ulcerative colitis (UC) and BP. The Phase 2 trial in UC is a randomized, double-blind, placebo-controlled, multi-center study that will evaluate the clinical efficacy and pharmacokinetic profile of bertilimumab in patients with active moderate to severe UC. Importantly, key inclusion criteria include high eosinophilia, as confirmed by eotaxin-1 levels (≥ 100 pg/mL) from a colon biopsy. The trial was initiated in February 2013 with results expected in late 2014 or early 2015. A potential Phase 3 development strategy will be to position bertilimumab as a first-line personalized therapeutic option for moderate to severe UC patients with high eotaxin-1 levels. To achieve this it will be necessary to show efficacy in two large pivotal Phase 3 trials that examine approximately 700 patients. We forecast the Phase 3 trials to commence in 2016 with potential approval by the FDA in 2019. We forecast peak sales of bertilimumab for UC as $2.5 billion.

The Phase 2 trial for BP is a safety and efficacy trial that will involve administration of bertilimumab at onset of the study and two weeks later with concurrent administration of low-dose prednisone. Efficacy, as assessed by a reduction in patients' symptoms, will be evaluated at week four. Positive results with no known safety issues will lead to a double-blind, placebo controlled Phase 3 trial. The primary endpoint of that trial would be remission as measured by a decrease in the number of blisters. Secondary endpoints could include a reduction in hospitalization and morbidity. The trial could be completed by the middle of 2016 with a possible FDA approval in 2017. Immune plans to seek orphan drug designation for bertilimumab in the treatment of BP. We believe that bertilimumab would command orphan pricing based on the fact there is no cure for BP and bertilimumab represents a potential paradigm shift in the treatment of BP. Due to this, even with the very limited potential patient population (~30k worldwide.), we forecast peak sales of bertilimumab for BP as $200 million.

Oral Amphotericin B Offers Upside Potential

iCo Therapeutics owns the worldwide exclusive rights to an oral Amphotericin B delivery system for life-threatening infections. The drug delivery technology also has the potential to re-profile other intravenously administered drugs to the oral route of administration.

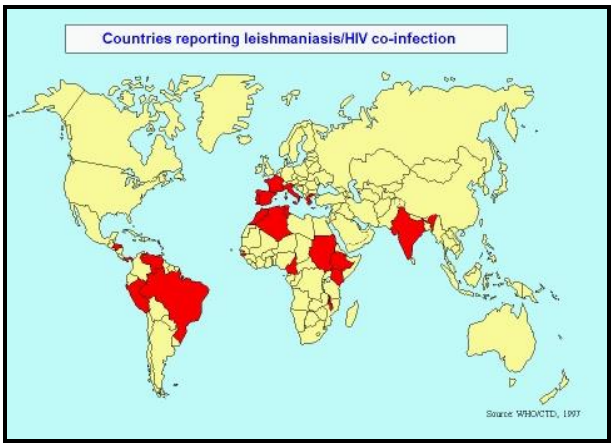
Amphotericin B (AmpB), the gold standard for systemic antifungal drugs, is one example of a well-established, highly efficacious systemic antifungal drug that has a 50-year history of intravenous therapy. The drug is highly potent and has utility as an anti-parasitic agent as well. Intravenous formulations such as AmBisome® and Fungizone® remain among the most effective agents in the treatment of life-threatening systemic fungal infections, including aspergillosis, cryptococcosis (torulosis), North American blastomycosis, systemic candidiasis, coccidioidomycosis, histoplasmosis, zygomycosis including mucormycosis due to susceptible species of the genera *Absidia, Mucor,* and *Rhizopus,* and infections due to related susceptible species of *Conidiobolus* and *Basidiobolus*, and sporotrichosis.

Surprisingly, no oral formulations of AmpB are currently commercially available. Although some patients are able to tolerate the IV injection, many experience localized and systemic side effects associated with intravenous administration of the drug. For example, the Side Effect & Drug Interactions section of the AmBisome® prescribing information includes warnings on renal impairment, hepatic impairment, febrile reactions, fever accompanied by shaking chilies, normochromic and normocytic anemia, musculoskeletal pain, anaphylactic reactions, dermatologic reactions, including Steven-Johnson syndrome, neurologic reactions, including convulsions, tinnitus, and vertigo, hematological reactions, and injection site reactions. Some of these side effects can be eliminated or reduced, specifically the injection site reactions and potentially the hematological, hepatic, and renal impairments, by oral administration. Sales of the perceived "least toxic" formulation of AmpB, AmBisome®, were $474 million in 2012.

Oral administration would also facilitate self-administration, allowing earlier hospital discharge where already immuno-compromised patients with cancer, organ transplant recipients, diabetics, and HIV/AIDS are susceptible to opportunistic hospital-based infections. We suspect an oral AmpB offers potential improvement in quality of life measures such as convenience as well. However, in developing nations, the need for oral therapies is not a matter of convenience, or cost for that matter, but instead is one of survival. The benefit of developing oral therapies is illustrated by the protozoan *Leishmania donovani*, an insidious parasite that is transmitted by the bite of an infected sand fly. It is the second largest parasitic killer after malaria. Sources estimate that visceral Leishmaniasis affects more than 100 million people worldwide, with 500,000 new cases and more than 50,000 deaths each year (Desjeux, P., 2004).

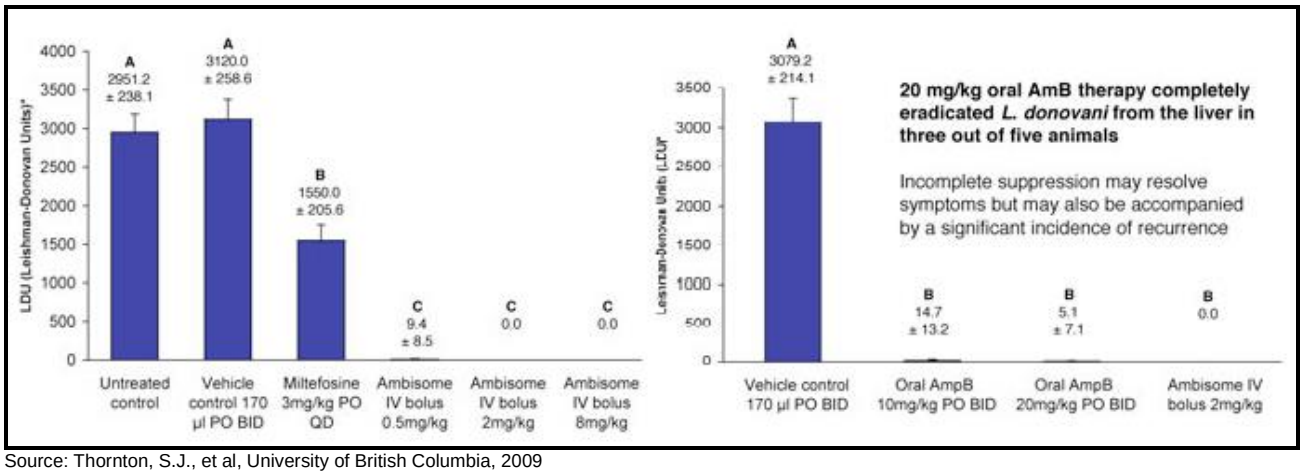
Although *Leishmania donovani* is only the second-most prevalent Leishmania causing parasite, it is the most dangerous form and directly fatal to humans if left untreated. Over 90% of reported cases are from India, Bangladesh, Nepal, Sudan and Brazil. In India, it is prevalent in the eastern region including Bihar, West Bengal, eastern Uttar Pradesh, Assam and foothills of Sikkim. It is responsible for tens of thousands of deaths among Africans in eastern and southern parts of Sudan (Wikipedia).

During the epidemic of 1984–1994 death toll was as high as 70% in the Sudanese population (Seaman J., et al, 1996). The emergences of drug resistant strains facilitate the spreading epidemic, and in fact Leishmaniasis is present in central Europe.



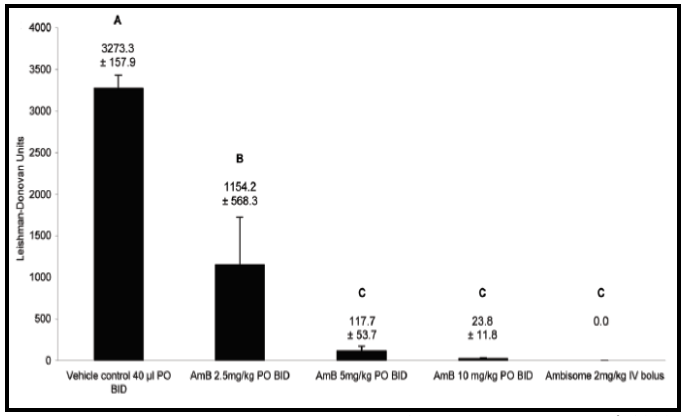
Source: Max Plank Institute, February 2000

The laboratory of Dr. Kishor M. Wasan of the University of British Columbia has made significant strides toward the development of a proprietary, lipid-based AmpB formulation for oral administration. Initial data from both cell lines and in vivo research indicate that it is highly efficacious and exhibits low toxicity within the dosage range required for the treatment of diseases such as disseminated fungal infections and Leishmaniasis. The graphs below show liver parasite load in Lesihmania-infected mice, untreated, treated with a sham vehicle control, and milefosine at 3 mg/kg, various concentrations of AmBisome®, and various concentrations of a development-stage oral AmpB formulation.



Source: Thornton, S.J., et al, University of British Columbia, 2009

In a similar study, BALB/c mice were treated with 2.5, 5, and 10 mg/kg oral AmpB BID for 5 days; a single 2 mg/kg IV dose of AmBisome; or a lipid-based vehicle control BID PO for 5 days (4 mice in each group). Different letters above bars indicate statistically significant differences between treatment groups; matching letters indicate groups with no statistically significant difference. Note how treatment with 2 mg/kg of intravenous AmBisome completely eradicated liver parasites one week after infection. The oral AmpB formulation tested resulted in 99.5% ± 0.4% and 99.8% ±0.2% reduction for the 10 and 20 mg/kg BID doses, respectively.



Source: Wasan, K.M. et al, 2009

…Development Plans…

iCo Therapeutics is developing a lipid capsule formulation of AmpB, iCo-009, where management uses the analogy of a "candy wrapper" around the active amphotericin molecule. Additional formulations molecules, iCo-010, also exist. The company acquired the exclusive worldwide rights to the drug back in May 2008 from the Wasan Lab at the University of British Columbia. To date, iCo Therapeutics has received a total of $2.0 million in on-dilutive grant funding from the Canadian government and Bill and Melinda Gates Foundation. The company has been using the funds for feasibility testing, further IND enabling studies, and clinical trials looking at iCo-009 as a possible treatment and cure for latent HIV-reservoirs.

In November 2013, U.S. patent #8,592,382 was issued for the Oral Amphotericin B platform providing protection around oral delivery of the drug. iCo Therapeutics has progressed into *in vitro* testing with study partners in Montreal, and will examine the role of this formulation in targeting latent HIV reservoirs which remain in individuals despite enormous therapeutic advances in the treatment of HIV/AIDS. *In Vitro* work from eight HIV-infected subjects successfully treated with highly active antiretroviral therapy (HAART) with detectable latent viral reservoir is expected to be complete in the first half of 2014.

In September 2010, iCo Therapeutics was granted Orphan Drug status by the U.S. FDA for the treatment of Visceral Leishmaniasis (VL). Orphan designation qualifies iCo for tax and marketing incentives, which can include tax credits for clinical research, study design support, exemption from application-filing fees, grant funding for clinical trials, and seven years of marketing exclusivity after the approval of the drug. As noted above, animal model studies from 2008 showed a >99% knock-down effect of parasitic infection caused by VL with 10 and 20 mg/kg of iCo-009 oral administration BID for one week.

Above we noted the drugs broad-scale use as a systemic antifungal agent. This presents additional development opportunities for iCo or a partner in the future.

MANAGEMENT BIO

Andrew J. Rae, MBA - President, CEO and Director

Mr. Rae is President, CEO, and co-founder of iCo Therapeutics, Inc. since inception in 2005. Mr. Rae has spent a decade in the biotechnology industry, formerly as CFO with Ability Biomedical Corporation (Irvine CA, Vancouver BC), acquired by Medarex, Inc. in 2004. Mr. Rae has also served as Vice President, Finance & Corporate Affairs at Active Pass Pharmaceuticals (Vancouver BC). In his various roles**,** Mr. Rae has raised approximately $50M in venture, strategic and capital markets financings**,** engaged in a successful cross-border M&A transaction, and played a significant role in shaping multiple business development deals (Cambridge Antibody, Isis Pharmaceuticals, Medarex). Prior to his operational experiences, Mr. Rae served as Biotechnology Equities Analyst, Goepel Shields & Partners (now Raymond James Canada), covering Canadian biotechnology stocks including Angiotech Pharmaceuticals, QLT Inc. and ID Biomedical. Mr. Rae currently sits on the Dean's External Advisory Board for the Faculty of Business Administration at Simon Fraser University, and the Board of Directors of Covenant House Vancouver, a charity operating shelters and counsel to homeless youth in Vancouver, BC. In 2009 Andrew was Pacific Finalist, Ernst & Young Entrepreneur of the Year (Canada). Mr. Rae's degrees include a B.Sc. from the University of Western Ontario and an MBA from Simon Fraser University.

Dr. Peter Hnik, MD, MHSc - Chief Medical Officer

Dr. Hnik received his medical degree from the Medical Faculty of Charles University of Prague in 1981. After practicing for years at the Eye Clinic of the Charles University Hospital where he performed surgery and consultation in glaucoma and neuro-ophthalmology, Dr. Hnik later joined the Eye Clinic of the University of British Columbia as part of the glaucoma research group. He received his Master of Health Sciences degree from the University of British Columbia in 1999. Prior to joining iCo Therapeutics, Dr. Hnik served as Associate Director of Clinical Research with QLT Inc., playing a critical role in designing and directing Visudyne clinical trials in AMD and diabetic retinopathy. He was also heavily involved in the publication, in-licensing and pharmacovigilance activities for Visudyne. He has authored numerous ocular publications and presentations at international forums. Dr. Hnik is a member of the Association for Research in Vision and Ophthalmology (ARVO), the American Academy of Ophthalmology (AAO), the European Society of Retina Specialists (EURETINA), the Drug Information Association (DIA), and the New York Academy of Sciences (NYAS).

W. John Meekison, BA, CIM - Chief Financial Officer

Mr. Meekison is a veteran investment banker specializing in life sciences at Loewen Ondaatje McCutcheon, Haywood Securities, Dlouhy Merchant and PI Securities. As a financier, Mr. Meekison has raised equity capital for various biotechnology companies such as StressGen Biotechnologies, ID Biomedical, Acorda Therapeutics, Inex Pharmaceuticals, Xenon Pharmaceuticals, Nortran Pharmaceuticals (now Cardiome) and BioMS Medical Corp. As CFO for a TSE listed company developing a novel clinical diagnostic platform, Mr. Meekison supervised all public reporting functions, human resources, accounting and budgeting, raising equity capital, renegotiating the Company's existing line of credit, reviewing corporate strategy, and led M&A discussions. Mr. Meekison sits on the Board of Directors of Pacific Cascade Minerals Inc., Ravenstar Ventures Inc., and Natcore Technology Inc. Mr. Meekison received his BA from the University of British Columbia and is a Certified Investment Manager.

William Jarosz, JD - Chairman of the Board of Directors

William Jarosz is currently a Partner at Cartesian Capital Group, LLC, a global investment management firm. From 1997 until 2005, Mr. Jarosz served as Managing Director and General Counsel of AIG Capital Partners, a subsidiary of American International Group, Inc., and as Managing Director of the AIG-Brunswick Millennium Fund. While at AIG Capital Partners, Mr. Jarosz oversaw global private equity transactions for the firm's various private equity funds. Prior to joining AIG in 1997, Mr.Jarosz practiced law at Debevoise & Plimpton, specializing in international private equity investment and Russian corporate and securities laws. Mr. Jarosz also served as a consultant to the World Bank on the regulation of Foreign Direct Investment in emerging markets. Mr. Jarosz is a graduate of the University of Montana, and received an MA in Law and Diplomacy from the Fletcher School at Tufts University and a JD from Harvard Law School.

Noel Hall, BSc – Director

Noel Hall is currently a consultant to the life sciences industry and has approximately 25 years of experience in the biotechnology industry, including as president of Aspreva Pharmaceuticals Corporation, which was acquired by the Galenica Group in January 2008. Prior to co-founding Aspreva in December 2001, Mr. Hall co-founded the life sciences practice of consulting firm Hill and Knowlton in 1995 and served as head of global strategic planning for the firm's worldwide pharmaceutical consulting practice. From 1992 to 1995, Mr. Hall was the director of corporate affairs for the United Kingdom and Northern Europe for The Wellcome Foundation Ltd., which is now part of GlaxoSmithKline PLC. From 1985 to 1990, Mr. Hall worked in market development with Abbott Laboratories Ltd. and from 1983 to 1985 Mr. Hall was a regional sales manager with Leo Laboratories Ltd. Mr. Hall holds a BSc in Medical Laboratory Science from London University.

Richard Barker, DPhil, BA – Director

Dr Richard W. Barker was Director General of the Association of the British Pharmaceutical Industry from August 2004 to May 2011. Prior to joining APBI, Dr. Barker was the Founder and President of New Medicine Partners, CEO of iKnowMed, Chief Executive of Chiron Diagnostics, General Manager of IBM's Worldwide Healthcare Solutions division, and leader of McKinsey's European healthcare practice. He is currently a board member of Celgene Corporation, the European Federation of Pharmaceutical Manufacturers and Associations (EFPIA) and council member of the international equivalent body (IFPMA). He also serves on the board of Adlyfe, a company specializing in protein misfolding diseases. Dr. Barker's academic background includes research in biological magnetic resonance at Oxford, Leeds and Munich. He holds a D.Phil in biophysics and a B.A. in chemistry, both from Oxford University.

Douglas G. Janzen – Director

Mr. Janzen was most recently President and Chief Executive Officer at Cardiome Pharma Corp. where he led all of the company's business activities, including capital markets, commercial development, and partnering, licensing and other strategic transactions. Doug joined Cardiome in 2003 as Chief Financial Officer and was instrumental in the advancement of the company's corporate development and the strengthening of its financial position. Prior to joining Cardiome, he served as Managing Director, Health Sciences and Partner at Sprott Securities, Inc., a Toronto-based investment bank.

VALUATION & RECOMMENDATION

Attracted To iCo Therapeutics

iCo Therapeutics shares currently trade with a market capitalization of only $30 million (for the U.S. OTCQX listed shares). There are four key points that lead us to delve deeper into the iCo story.

- ✓ Firstly, in November 2013, the company saw the final exercising of roughly 3.207 million warrants at $0.30 dating back to the November 2011 financing, raising gross proceeds of approximately $0.962 million. We were pleased to see the company pull in this extra cash with existing investors.
- ✓ Secondly, in December 2013, the company's shares began trading on the OTCQX, the highest tier of the OTC Market, under the ticker symbol: ICOTF. We believe the QX listing will help iCo Therapeutics gain greater exposure and increased liquidity with biotech investors in the U.S.
- ✓ Thirdly, in late January 2014, the company raised gross proceeds of CAD$6.75 million through the issuance of 16.206 million shares of common stock at $0.4165 per share. We modeled that iCo Therapeutics exited 2013 with roughly $1.5 million in cash. Adding into this new net $6.3 million cash from the equity financing should put cash and investments at roughly $6.0 million as of March 31, 2014. This effectively eliminates any new financing risk prior to the release of the iDEAL data and creates a clear catalyst to our fourth key point. We note that previous investors in the company, the Special Situations Fund III QP, L.P. and Special Situations Life Sciences Fund, L.P., increased their position in this offering and now own 16.5% of the outstanding shares.
- ✓ Fourthly, top-line results from the iDEAL study are expected in April 2014, creating a clear valuation inflection point for investors if the data are positive.

…Value Heavily Dependent On iDEAL…

Our analysis of iCo-007 began with a thorough analysis of antisense drug development, and that acknowledgement antisense technology has not lived up to the hype that ensued over two decades ago when the technology was first brought public. Nevertheless, through trial and error, it now seems abundantly clear that success of an antisense drug is dependent on delivery and target location. For iCo, delivery of an antisense drug through intravitreal injection has been fully validated from a clinical and commercial standpoint by the approval and launch of Vitravene at Novartis. Treatment of DME represents a large market opportunity, and the mechanism of action of the current leading therapies, anti-VEGF, has been proven highly successful by intravitreal injections of drugs like Avastin®, Lucentis®, and Eylea®. More specifically, however, the mechanism of action of iCo-007, upstream blockage of the protein kinase, c-Raf, a signal transmitter for VEGF and other growth factors, hold significant scientific merit (1, 2, 3, 4, 5). Our analysis of published literature leads us to conclude that the Raf genes play an important regulatory roles in signal transduction processes that regulate cell proliferation and angiogenesis. Patents have been awarded protecting such technology, and preclinical and Phase 1 data yield highly encouraging results for iCo-007.

In March 2012, iCo Therapeutics initiated enrollment in iDEAL (NCT01565148), a Phase 2 study designed to explore whether varying combinations and concentrations of iCo-007 are effective in improving visual acuity in people with diabetic macular edema. The trial is co-sponsored by the Juvenile Diabetes Research Foundation. In iDEAL, patients will receive repeated intravitreal injections of iCo-007 as a monotherapy and in combination with ranibizumab (Lucentis®) or laser photocoagulation, randomized into one of four treatment groups noted below:

1. Intravitreal dosing of 350 µg iCo-007 at baseline and Month-4
2. Intravitreal dosing of 700 µg iCo-007 at baseline and Month-4
3. Intravitreal dosing of 350 µg iCo-007 at baseline + laser photocoagulation Day-7, then another intravitreal dosing of 350 µg iCo-007 at Month-4 + laser photocoagulation at seven days later (if necessary).
4. Intravitreal dosing of 0.5 mg ranibizumab (Lucentis®) at baseline + 350 µg iCo-007 at Day-14, then a repeat dose of 0.5 mg ranibizumab at Month-4 + 350 µg iCo-007 14 days later.

The primary endpoint of the iDEAL study is mean change in visual acuity (VA) from baseline to month eight. Safety outcome measures include the number of participants in a given study arm experiencing the same drug-related serious adverse event as a measure of safety and tolerability at month 12 and safety of repeated iCo-007 intravitreal injections in treatment of subjects with DME as monotherapy and in combination with ranibizumab or laser photocoagulation throughout the entire study.

Secondary outcome measures include change in VA from baseline to month 12, change in retinal thickness measured by OCT from baseline to month eight and 12, duration of iCo-007 treatment effect during the 12 month follow-up period as measured by VA and OCT thickness, and then peak plasma concentration (C_{MAX}) of iCo-007 after multiple injections.

The mid-point of the trial was reached in January 2013, and the company announced no serious drug-related adverse events among patients receiving repeat doses of iCo-007. In June 2013, the company announced that enrollment was completed at 187 patients randomized. Recruitment took place at 28 clinical sites across the United States. The iDEAL study is a multi-center study chaired by Quan Dong Nguyen, MD, MSc, Professor and Chair of Ophthalmology and Director of the Stanley M. Truhlsen Eye Institute at University of Nebraska Medical Center (UNMC).In addition, the Retinal Imaging Research and Reading Center (RIRRC) based at the UNMC serves as the Reading Center for the iDEAL Study. Top-line data from the primary endpoint at month eight are expected in April 2014. Full data at month twelve is expected in September or October 2014.

For the purpose of establishing valuation of iCo Therapeutics, we estimate 50% likelihood that the iDEAL trial will demonstrate acceptable safety and an efficacy profile comparable to Lucentis® after eight months (two doses). The results from the Eylea® VISTA-DME study have set the bar high. However, the potential for less frequent dosing (quarterly vs. monthly or every other month) present a very interesting market share grabbing opportunity if iCo-007 can demonstrate 10-12 lines of improvement on BCVA similar to Eylea®. However, other interesting development pathways exist for iCo Therapeutics should the results fall shy of Eylea's impressive data from VISTA. Specifically, results in anti-VEGF non-responders will be very important for the future development of the drug. Research shows that approximately 30-40% of DME (and AMD) patients are non-responders to drugs like Lucentis® and Eylea®.

For iCo Therapeutics, the pending results of the iDEAL study represent a major potential inflection point in the company's valuation. If results from iDEAL are positive, iCo is sitting on a potential $1+ billion drug. A label for anti-VEGF non-responders still offers a potential $500 million opportunity. Assuming a path forward, we believe that the company will likely seek a development partner for the U.S. Phase 3 registration program. Such a deal may be signed with $50 million in upfront licensing payments to iCo Therapeutics, with a potential backend regulatory and sales milestone pot totaling $500 million. We also project any such deal would pay iCo a tiered royalty on sales, ranging from the low-teens to low-twenty percent from the commercialization partner.

Assuming U.S. approval in 2018, with the aforementioned peak sales of $1 billion and the out-licensing terms outlined above, with 50% likelihood of a positive iDEAL trial and a 25% discount rate, we see the iCo-007 NPV at $80 million. Gaining of additional patent applications that extend exclusivity of the molecule beyond 2023 could add as much as $50 million in value to our NPV calculation. We remind investors that our NPV calculation factors in terms of the original license agreement with ISIS back in 2005, and includes up to $22 million in developmental milestones and an unspecified royalties on sales (which we model at 6%).

…iCo-008 & iCo-009 Represent Meaningful Upside…

Beyond iCo-007 and the pending outcome of the iDEAL study, iCo Therapeutics has two other potential revenue drivers that warrant inclusion in our sum-of-parts valuation model. The first is iCo-008, a first-in-class fully human IgG4 monoclonal antibody discovered using Cambridge Antibody Technology's phage display technology, and licensed to iCo in January 2007. The mechanism of action of iCo-008, also known as bertilimumab, has been described in detail by numerous authors in peer-reviewed papers we reviewed for preparation of our report.

Preclinical work show high affinity and specificity for eotaxin-1, a pro-inflammatory cytokine that plays a critical role in mast cell degranulation and the development of an inflammatory condition known as eosinophilia. Clinical and preclinical evidence proves that by blocking eotaxin-1 can result in effective inhibition of early phase mast cell activation as well as late phase eosinophilia. iCo Therapeutics believes this mechanism of action has clinical utility for the treatment of vernal keratoconjunctivitis (VKC) and wet age-related macular degeneration (AMD).

Beyond ocular indications, iCo Therapeutics has out-licensed bertilimumab to Israeli-based Immune Pharmaceuticals (IMNP) for the treatment of Irritable Bowel Disease (IBD) and Bullous Pemphigoid (BP). The clinical data in all indication is a little early-stage, and thus forecasting potential peak sales and probabilities of approval is difficult. However based on modest success in VKC and/or AMD, and similar blockbuster success by Immune Pharma in IBD or BP, we think iCo-008 is worth $25 million.

iCo Therapeutics also owns the worldwide exclusive rights to an oral Amphotericin B delivery system for life-threatening infections. Amphotericin B (AmpB), the gold standard for systemic antifungal drugs, is one example of a well-established, highly efficacious systemic antifungal drug that has a 50-year history of intravenous therapy. iCo's candidate is the company's oral lipid capsule formulation of AmpB. The company acquired the exclusive worldwide rights to the drug back in May 2008 from the Wasan Labs at the University of British Columbia. In November 2013, U.S. patent #8,592,382 was issued for the Oral Amphotericin B platform providing protection around oral delivery of the drug.

iCo Therapeutics has progressed into *in vitro* testing with study partners in Montreal, and will examine the role of this formulation in targeting latent HIV reservoirs which remain in individuals despite enormous therapeutic advances in the treatment of HIV/AIDS. Recruitment of eight HIV-infected subjects successfully treated with highly active antiretroviral therapy (HAART) with detectable latent viral reservoir is expected to be complete in the first half of 2014. In September 2010, iCo Therapeutics was granted Orphan Drug status by the U.S. FDA for the treatment of Visceral Leishmaniasis (VL).

Orphan designation qualifies iCo for tax and marketing incentives, which can include tax credits for clinical research, study design support, exemption from application-filing fees, grant funding for clinical trials, and seven years of marketing exclusivity after the approval of the drug.

As noted above, animal model studies from 2008 showed a >99% knock-down effect of parasitic infection caused by VL with 10 and 20 mg/kg of iCo-009 oral administration BID for one week. We have assumed very modest success for iCo-009 in our valuation model, concluding that without more substantial human clinical data, the candidate is worth roughly $10 million in value.

iCo Therapeutics: Sum-Of-Parts Analysis	
iCo-007	**$80 Million**
iCo-008	**$25 Million** [A]
iCo-009	**$10 Million**
Cash & Investments	**$8.0 Million** [B]
Operating Burn	**($20.0 Million)**
Total Firm Value	**$103 Million**
Fully Diluted Shares	**114.6 Million** [C]
Target Price	**$0.90 / Share**

A = Includes interest in Bertilimumab at Immune Pharma
B = Includes ownership in Immune Pharma
C = Includes Basic shares + all outstanding stock options and warrants

iCo Therapeutics shares are currently trading with a market value of only $45 million on a fully-diluted basis (based on $0.40 per share). Chief competitors in this space, Ohr Pharmaceuticals, Alimera Sciences, and pSivida Corp are all trading at significant premiums to iCo.

Competitor Comp	Market Value [A]
Ohr Pharmaceuticals, Inc.	$311 Million
Alimera Sciences, Inc.	$222 Million
pSivida Corp.	$126 Million
Lpath, Inc.	$61 Million
Ophthotech Corp.	$1,120 Million
AVERAGE	**220 Million** [B]
iCo Therapeutics	**$30 Million**
Upside	**+ 633%**

A = As of February 21, 2014
B = Excludes high (Ophthotech) and low (Lpath)

Sum-of-parts analysis tells us that iCo's stock has 125% upside based on a 50% probability of success of iDEAL in April 2014. Comparator analysis tell us that the shares could be worth as much as $3.00, or +633% upside, if iDEAL hits on the full data analysis in September / October 2014. As such, we see meaningful upside in owning the stock at this level.

Risks To Consider

Despite what we see as a meaningfully undervalued stock, there are certain risks to consider prior to an investment in iCo Therapeutics shares.

→ iCo-007 Fails: The primary risk for investors in buying iCo Therapeutic stock prior to the release of the top-line data from the iDEAL study in April 2014 is that the drug fails to demonstrate meaningful efficacy on BCVA when compared to Lucentis® or Eylea®. iCo-007 represents $80 million in our sum-of-parts valuation analysis. Failure of the drug would force us to slash our price target to $35 million on a fully-diluted basis. This equates to $0.30 per share. We suspect the shares may trade below this level given that in our conversations with investors, limited value at all is being assigned to iCo-008 or iCo-009.

→ New competition: Ohr Pharmaceuticals is developing Squalamine, an anti-angiogenic twice weekly eye drop currently in a Phase 2 study for the treatment of AMD, with future plans to expand into DME if it works. Squalamine's mechanism of action is similar to Lucentis® and Eylea® in its targeting of VEGF, PDGF, and other growth factors that lead to angiogenesis. The clear benefit of self-administered eye drops vs. once weekly, bi-weekly, or even monthly intravitreal injections by an ophthalmologist cannot be overstated. The data on Squalamine remains early-stage. However, if successful and eventually commercialized, the drug could dominate the market with similar efficacy to the anti-VEGF drugs like Lucentis® and Eylea®.

Ohr Pharmaceuticals has an impressive Ophthalmic Advisory Board, which includes David Boyer, MD who published on iCo's preclinical and Phase 1 data. We suspect that if Squalamine shows promise in the ongoing Phase 2 study, designed as a rescue therapy assessment for new AMD patients on Lucentis®, Squalamine could end up in the hands of a major player in the ophthalmology field.

→ New Financings: We model iCo Therapeutics exiting the calendar first quarter 2014 with roughly $6.0 million in cash. The company's stock in now publicly traded Immune Pharma is worth another $2+ million. With an operating burn of around $1.5 million per quarter, we believe iCo will require new cash to fund operations later in 2014. If the top-line results from iDEAL are positive, we suspect that iCo will be able to secure new funding at meaningfully higher levels. However, we do not believe the company will be able to secure a development partnership for iCo-007 until after the full results from iDEAL have been presented, which is expected to take place in September or October 2014. This is around the time we suspect the company will require new cash if they do not act on the top-line results from iDEAL this spring or summer.

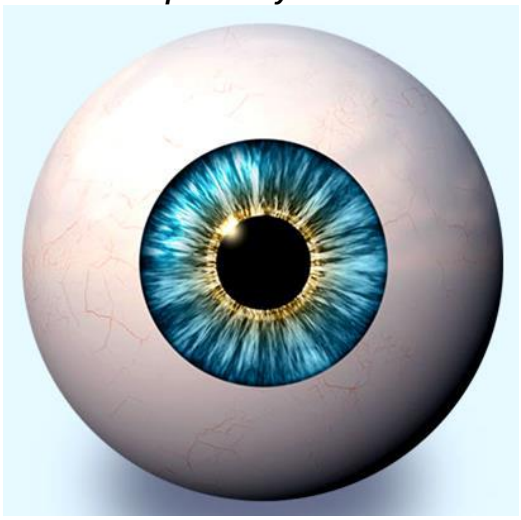
Conclusion & Recommendation

Sum-of-parts modeling calculates that iCo Therapeutics shares are meaningful undervalued at today's market value of only $45 million on a fully diluted basis. We note this value includes some 28.6 million warrants at or very near in-the-money. These warrants have the potential to provide another $10+ million in cash to the company if exercised. On a basic share count, iCo's market value is a bafflingly low $32 million.

Our analysis finds that the shares should be valued more in the $100-105 million range, or around $0.90 per share on a fully-diluted basis. This represents tremendous upside to investors at today's price of only $0.38 per share. However, investors need to be aware that approximately 80% of our valuation is coming from iCo-007 for the treatment of DME (and off-label use in AMD). We expect top-line results from the iDEAL study are expected in April 2014.

Despite what we see as a substantially undervalued story, we do see downside risk on the failure of the iDEAL trial in April 2014. But, we are not opposed to buying the stock at today's price ahead of the results. At the very least, we expect interest in the story to gain steam as we get closer to the announcement. We believe results from iDEAL in April 2014 could go one of three ways. They could be fantastic, meaning efficacy on par with Lucentis® or Eylea® coupled with improved safety and less frequent dosing. We believe this could re-value the shares at $2 rather quickly. They could be mixed, meaning efficacy short of the Eylea® VISTA-DME data but with subset analysis showing strong benefits in anti-VEGF non-responders. We believe this could re-value the shares at $1. Or they could disappoint, putting the shares down to the $0.20 area.

Keep Your Eye On iCO



It is clear there is dramatically more upside in the shares based on the results of iDEAL than downside. This type of favorable risk / reward should be attractive to most investors. However, after the iDEAL results the risk / reward should be even more favorable. The reward may not be as great, for example investors may have to buy the stock at $0.50 or $0.75 after the results if they are positive, but the risks of a failure will be removed. We see iDEAL as a potential game-changer for iCo Therapeutics.

We believe there will be a substantial multi-month run in the shares to the full data in September / October 2014 if the top-line results look solid. So we would advise keeping an eye on the shares for the top-line results in April 2014. A prudent strategy might be to establish a small position (25% to 50%) today, and then fill the rest of the order if the data from iDEAL is April 2014 impresses. Thus, our rating is **Outperform**.

PROJECTED FINANCIALS

iCo Therapeutics Inc.
Income Statement

iCo Therapeutics, Inc.	2012 A	Q1 A	Q2 A	Q3 A	Q4 E	2013 E	Q1 E	Q2 E	Q3 E	Q4 E	2014 E	2015 E	2016 E
iCo-007	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-
iCo-008	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-
iCo-009	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenues	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$5.000	$5.000
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-	-	-	-	-	-
Research & Development	$2.287	$1.199	$0.991	$1.368	$1.500	$5.058	$1.600	$1.650	$1.650	$1.550	$6.450	$6.500	$7.000
General and Administrative	$1.375	$0.626	$0.540	$0.423	$0.550	$2.139	$0.550	$0.550	$0.600	$0.650	$2.350	$2.500	$2.650
Foreigh Exchange	(0.007)	$0.038	$0.085	$0.015	$0.020	$0.158	$0.020	$0.020	$0.020	$0.020	$0.080	$0.090	$0.100
Operating Income	($3.654)	($1.863)	($1.616)	($1.806)	($2.070)	($7.356)	($2.170)	($2.220)	($2.270)	($2.220)	($8.880)	($4.090)	($4.750)
Operating Margin	-	-	-	-	-	-	-	-	-	-	-	-	-
Interest Income	$0.01	$0.000	$0.005	$0.004	$0.005	$0.013	$0.005	$0.005	$0.005	$0.005	$0.020	$0.020	$0.020
Other Income	$0.00	$0.041	$0.042	($0.041)	$0.040	$0.082	$0.040	$0.040	$0.040	$0.040	$0.160	$0.150	$0.150
Investments	$0.00	$0.031	$0.798	($0.490)	$0.200	$0.540	$0.250	$0.250	$0.250	$0.250	$1.000	$1.00	$1.00
Pre-Tax Income	($3.64)	($1.790)	($0.772)	($2.334)	($1.825)	($6.721)	($1.875)	($1.925)	($1.975)	($1.925)	($7.700)	($2.920)	($3.580)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0.00	$0.00	$0.00
Tax Rate	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Net Income	($3.64)	($1.790)	($0.772)	($2.334)	($1.825)	($6.721)	($1.875)	($1.925)	($1.975)	($1.925)	($7.70)	($2.92)	($3.58)
Net Margin	-	-	-	-	-	-	-	-	-	-	-	-	-
Reported EPS	($0.07)	($0.03)	($0.01)	($0.04)	($0.02)	($0.11)	($0.02)	($0.02)	($0.02)	($0.02)	($0.09)	($0.03)	($0.04)
YOY Growth	-	-	-	-	-	$0.50	-	-	-	-	($0.15)	($0.65)	$0.10
Basic Shares Outstanding	49.50	51.38	54.76	58.03	80.00	61.04	81.00	82.00	83.00	84.00	82.50	90.00	100.00

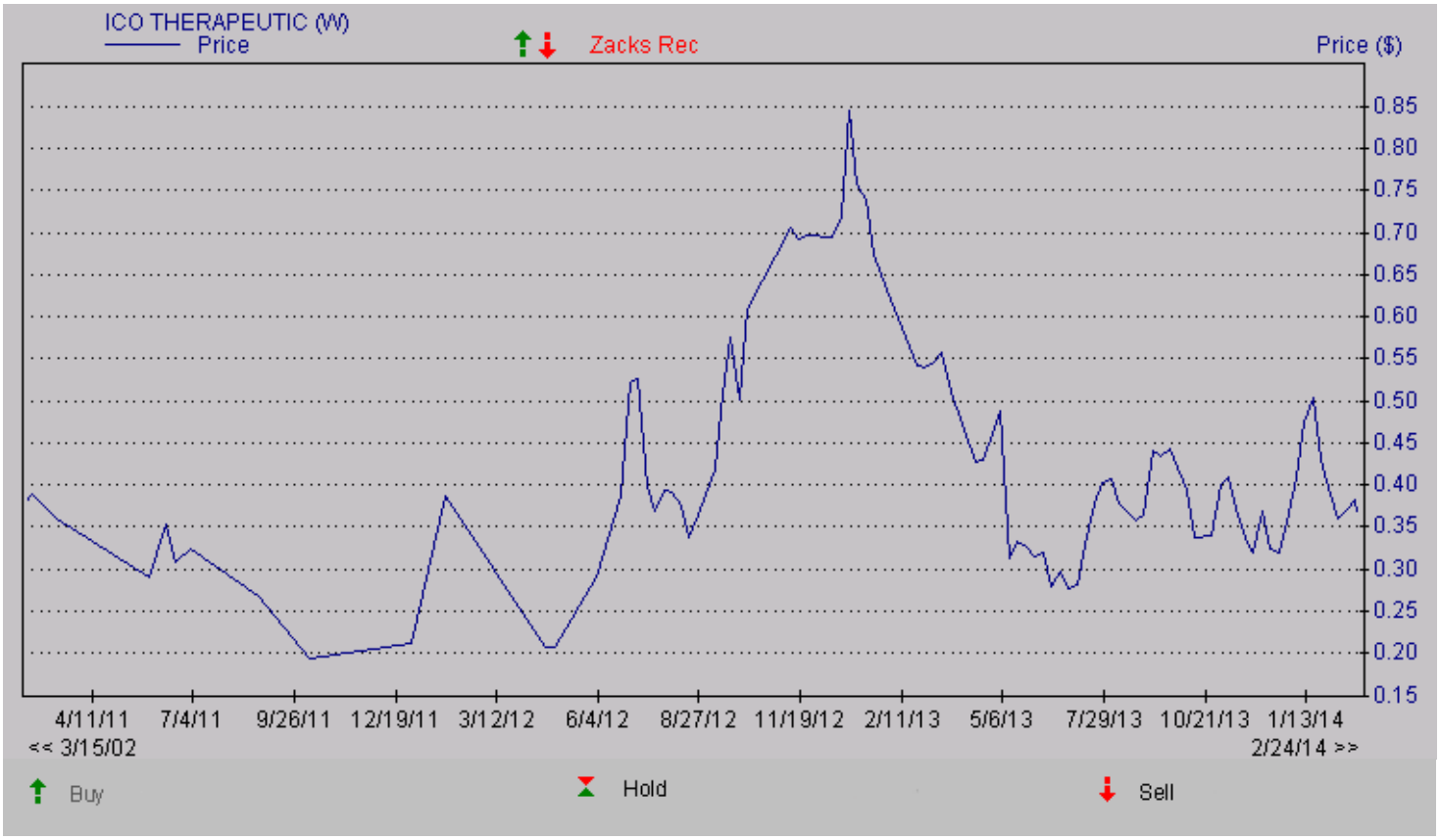
Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

iCo Therapeutics Inc.
Balance Sheet

(in Canadian dollars)

	Note	September 30, 2013 $	December 31 2012 $
Assets			
Current assets			
Cash and cash equivalents		644,204	599,457
Short-term investments		1,498,796	660,739
Other investments	3	1,447,633	-
Taxes and other receivables		9,441	25,118
Deferred financing		22,604	22,604
Prepaid expenses		17,779	30,934
		3,640,457	1,338,852
Other investments	3	-	1,432,657
Equipment		7,025	8,125
Intangible assets		163,317	233,801
		3,810,798	3,013,435
Liabilities			
Current liabilities			
Accounts payable and accrued liabilities	4	2,852,676	963,731
Shareholders' Equity			
Capital stock	5	22,730,229	19,978,848
Contributed surplus	5	3,036,579	2,403,324
Warrants	5	1,303,483	559,083
Accumulated other comprehensive (loss) income		(659,422)	250,776
Accumulated deficit		(25,452,747)	(21,142,327)
		958,122	2,049,704
		3,810,798	3,013,435

HISTORICAL ZACKS RECOMMENDATIONS



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Sell/Underperform: The analyst expects the company will underperform the broader U.S. Equity market over the next one to two quarters.

The current distribution is as follows: Buy/Outperform- 17.7%, Hold/Neutral- 75.5%, Sell/Underperform – 6.2%. Data is as of midnight on the business day immediately prior to this publication.