

LPATH, INC. (OTCBB: LPTN)

EXCITING iSONEP™ RESULTS ENHANCE LPATH'S OPHTHALMIC FRANCHISE

- ❑ **PHASE I iSONEP™ RESULTS IN WET AMD PATIENTS IMPRESSIVE.** In its Phase I trial, iSONEP met its primary endpoint of being well tolerated at all dose levels. Of particular interest, significant biological benefit was observed during the 30-40 days following just a single injection in all five of the patients with an "occult choroidal neovascularization (CNV)" present. The average reduction in CNV lesion size was 77% for this group of patients, and, for the two that had retinal pigment epithelium (RPE) detachment, the condition was virtually resolved within 45 days. Neither Lucentis® nor Avastin® typically show this type of clinical benefit with a single dose; in fact, in the MARINA Phase 3 trial, Lucentis-treated patients with occult disease experienced an average of 3% reduction in lesion size after 12 monthly injections. These results underscore the potential value of iSONEP's anti-inflammatory and anti-fibrotic mechanisms of action, which are non-overlapping and independent from the anti-VEGF therapies.
- ❑ **ASONEP™ SAFE AND WELL TOLERATED IN THE PHASE I SOLID TUMOR STUDY.** Expect ASONEP™ to be advanced in a Phase II involving patients with renal cell carcinoma and later to expand its clinical utility to other types of cancer. Merck-Serono currently holds the exclusive worldwide license to ASONEP™;
- ❑ **LPATHOMAB™ IS A PROMISING ASSET - POTENTIALLY APPLICABLE TO FIBROTIC DISORDERS, CANCER, AND PAIN MANAGEMENT;** and
- ❑ **SELF-GENERATING PIPELINE: LPATH'S IMMUNEY2™ PLATFORM IS A GOLDEN GOOSE THAT GENERATES NOVEL DRUG CANDIDATES.**

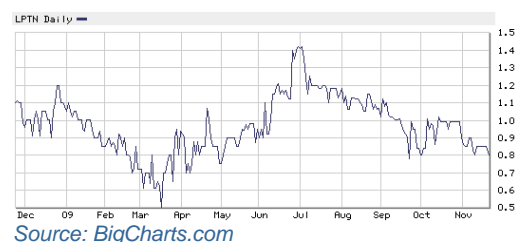
Lpath, Inc. (OTCBB: LPTN) is a biotechnology company focused on lipidomics-based therapeutics that target bioactive signaling lipids for treating a wide range of human disease. Lpath is the only company to have developed monoclonal antibodies against bioactive lipids. The Company has approximately 31 patents that either have been issued or are pending in the United States, with corresponding coverage in the international arena. The Company is currently advancing three drug candidates: ASONEP™; iSONEP™; and Lpathomab™. Lpath also has a drug-discovery engine called ImmuneY2™ which Lpath is leveraging to further expand its pipeline.

Pipeline:

- ASONEP for cancer (partnered with Merck-Serono): Phase I nearly complete in solid tumors; renal cell carcinoma (kidney cancer) shows promising FDA pathway.
- iSONEP for wet AMD: Phase I enrollment complete – Results compelling – both in terms of safety and biological effect.
- Lpathomab in early stage development, likely to be pursued in fibrotic disorders.
- New antibodies (Nextomabs), most likely targeting cancer and inflammatory diseases.

Share Price (11/20/09)	\$0.80
52-Week Price Low / HIGH	\$0.40 – \$1.47
Mkt. Capitalization (issued)	\$42.4 MM
Shares Outstanding (issued)	52.97 MM
12-month Target Price	\$5.00
Cash & Equivalents (9/30/09)	\$ 6.45 MM
Fiscal Year Ends	December 31st
Website	lpath.com

12-Month Price Chart



We are updating coverage on Lpath, Inc. (OTCBB: LPTN) with a BUY rating and a 12-month price target of \$5.00 for LPTN shares.

CHRISTYNA BEDRIJ 212-509-9500 CBEDRIJ@GRIFFINSECURITIES.COM	MARK MERRILL 646-442-1441 MMERRILL@GRIFFINSECURITIES.COM	KEITH MARKEY, PH.D. 212-514-7914 KMARKEY@GRIFFINSECURITIES.COM
--	---	---

HIGHLIGHTS

- **ISONEP PHASE I TRIAL SHOWS PROMISING RESULTS IN WET AMD.** iSONEP completed enrollment in its Phase I study and was well tolerated at all dose levels tested, and no drug-related serious adverse events were reported. Importantly from a potential commercial perspective, iSONEP was providing improvement in these patient's eyes with non-overlapping effect with the VEGF inhibitors (Lucentis and Avastin, and, if approved, the VEGF-Trap). Anti-fibrotic and anti-inflammatory effect may bestow iSONEP with significant therapeutic advantages over other ocular treatments that target single pathways, such as these anti-VEGF treatments. We expect iSONEP to be developed first for wet AMD, and then later expand its utility in other indications, such as diabetes- and glaucoma-related disorders, proliferative vitreoretinopathy (PVR), and possibly dry AMD.
- **ISONEP: LARGE COMMERCIAL OPPORTUNITY IN OCULAR INDICATIONS.** AMD is a leading cause of blindness in adults over 55 years of age. An estimated 15 million people in the United States have age-related macular degeneration (AMD), with more than 1.6 million experiencing the active blood vessel growth and blood vessel leakage associated with wet AMD with the numbers expected to climb. It is projected that, by the time iSONEP is introduced and ramping its sales volume, there will be 5 million wet AMD patients worldwide. With such a sizeable market opportunity, a company like Lpath can stratify the market (e.g., by focusing on occult patients only, which represent approximately 65% of the overall wet AMD market) and still end up with a multi-billion-dollar drug. Given iSONEP's multiple anti-inflammatory, anti-fibrotic and anti-angiogenic properties are non-overlapping with Lucentis and Avastin, and could provide efficacy improvement when utilized in combination with either treatment, we are enthusiastic about its commercial potential.
- **PHASE IA STUDY SHOWS EARLY PROMISE FOR ASONEP.** ASONEP's Phase Ia dose escalation study (15 evaluable patients) showed good tolerability and no drug-related serious adverse events. A Phase Ib extension (6-7 patients) is also nearly complete (3-4 renal cell carcinoma (RCC) patients, all at 24 mg/kg). Lpath's partner for the ASONEP™ program is Merck-Serono, a division of **Merck KGaA (XETRA: MRK)**. On September 24, 2009, Lpath announced that Merck-Serono extended the final option decision date to June 27, 2010.¹ For each month during the extension period before a final decision is made, we expect Lpath will receive \$500,000. If Merck-Serono elects to exercise the option to take control of the program, Lpath will receive a payment of \$28 million from Merck-Serono, who would assume any future development costs related to ASONEP, and, assuming commercialization, would then pay a royalty based on total product sales. We believe that although the program is progressing as planned (e.g., good safety and tolerability in Phase I) given Merck's recent early pipeline success on their own internal programs, they may choose to renegotiate the timing and/or terms of the original option with Lpath. In the meantime, the program continues to be funded by Merck (over \$12 million of non-dilutive payments made to Lpath thus far) and given that the initial data is showing promise (i.e., RCC) and patent estate unique and sound, whether or not Merck exercises its option to take control of the program, we believe the franchise is of considerable value to Lpath.
- **ASONEP USED TO TREAT RCC AS A SINGLE AGENT COULD PROVIDE A MUCH FASTER AND MORE STRAIGHTFORWARD FDA PATHWAY TO MARKET APPROVAL.** Proof-of-principle data presented in April at the 100th Annual Meeting of the American Association for Cancer Research (AACR) demonstrated that ASONEP administered as a single agent delayed the progression of renal cell carcinoma (RCC) by about 60% longer than the delay typically seen in this same model with VEGF-receptor-tyrosine-kinase inhibitors (TKIS). Sutent® and Nexavar®, the two approved TKIs, generated over \$1.5 billion in total sales in 2008. The encouraging RCC data is also typical of a potential combination treatment. ASONEP used in combo with current standards of care, including Avastin®, is likely to delay time of progression of disease. This suggests ASONEP could be used to treat RCC as a single agent, providing a much faster and more straightforward FDA pathway to market approval. We expect ASONEP™ to be advanced in a Phase II involving patients with renal cell carcinoma and later to expand its clinical utility to other types of cancer.

¹ Lpath, Inc. press release, "Lpath and Merck Serono Extend ASONEP™ Collaboration." Sep. 24, 2009.

- ❑ **LPATHOMAB: LPATH'S NEXT LIPID-TARGETING ANTIBODY.** Lpathomab binds to another important bioactive lipid, lysophosphatidic acid (LPA). LPA is known to promote cancer growth and metastasis of many different types of tumors and to serve as an integral element in the pathogenesis of neuropathic pain, as well as fibrotic and inflammatory diseases. Given the strong evidence of LPA's involvement in abnormal fibrosis, we believe Lpath will select a fibrotic disease for commercialization of Lpathomab. Lpath plans to explore the use of Lpathomab in fibrosis in the next 12 months and to submit an IND in at least one indication in 2011. Lpathomab also has potential in cancer; compelling results presented at the 100th AACR meeting in April 2009 demonstrated tumor progression inhibition in ovarian cancer. Lpathomab inhibited the progression of human ovarian tumor cells injected into mice. In addition to inhibiting tumor progression, Lpathomab blocked tumor-cell migration and reduced levels of pro-metastatic factors in the tumor models.²
- ❑ **SELF-GENERATING PIPELINE: LPATH'S LIPIDOMICS-BASED IMMUNEY2™ PLATFORM CONTINUES TO HOLD GREAT STRATEGIC VALUE AS A GOLDEN GOOSE THAT GENERATES NOVEL DRUG CANDIDATES.** Lpath's ImmuneY2 platform provides a in-house platform that generates novel drug candidates. Utilizing its ImmuneY2 platform technology, Lpath is the only company to have developed mAbs against bioactive lipids, making them the undisputed category leader. The ImmuneY2 platform, should provide Lpath with a robust and ever-growing pipeline of antibodies against novel targets. According to the British Journal of Cancer, the lipidome (the entire spectrum of lipids), contains 1,000 or more potential therapeutic targets.³
- ❑ **NCI GRANT A NON-DILUTIVE WIN.** On June 4, 2009, Lpath announced a three-year \$3 million grant from the National Cancer Institute's Small Business Innovation Research (SBIR) Program. The funds will support the continued clinical development of Lpath's leading drug candidate ASONEP. We believe that Lpath has the potential to receive additional grants from SBIR, which serve as a valuable non-dilutive financing for its clinical development programs.
- ❑ **LPATH'S ANTIBODIES ARE PROTECTED BY AN EXTENSIVE PATENT PORTFOLIO.** The Company has 31 U.S. patents, which either have been issued or remain pending, and corresponding coverage internationally. Notably, the patent portfolio – with respect to sonpecizumab – includes various composition-of-matter patents, as well as the recently issued U.S. patent #7,169,390 titled, "Compositions and Methods for the Treatment and Prevention of Cancer, Angiogenesis, and Inflammation," which broadly relates to methods of treating cancer using an antibody against S1P.
- ❑ **LPTN SHARES UNDERVALUED.** Lpath is the category leader in lipidomics-based therapeutics, an emerging field of medicine that targets bioactive signaling lipids for treating a wide range of human diseases, including cancer, ocular disorders, and certain inflammatory, cardiovascular, and fibrotic disorders. Recent exciting results in the iSONEP ophthalmic franchise, two Phase II-ready programs, and a validated platform solidifies Lpath's position in the marketplace. During 2009, the Company advanced its drug development programs for cancer and ocular disorders:
 - 1) Following its Phase I trial, iSONEP displayed exciting results, meeting its primary endpoint of being well tolerated at all dose levels, as well as showing significant biological benefit in patients with occult choroidal neovascularization (CNV) present, reducing the average CNV size by 77%, underscoring the potential value of iSONEP's anti-inflammatory and anti-fibrotic mechanisms;
 - 2) ASONEP's Phase Ia showed good safety and tolerability and is expected to be advanced in a Phase II involving patients with renal cell carcinoma (RCC);
 - 3) Lpathomab, Lpath's third program, continued to be evaluated in various models of cancer and fibrosis, is expected to move into the clinic in a lead indication in 2011; and
 - 4) In addition, the ImmuneY2 platform is generating additional mAbs against undisclosed lipid targets that should provide an ever-growing pipeline of novel, mAb-based drug candidates.In summary, our valuation model, based on projected sales of ASONEP, iSONEP, and Lpathomab, supports a 12-month target price of \$5.00 per share; therefore, we reiterate our BUY recommendation on Lpath, Inc. and establish a new 12-month target price of \$5.00 per share for LPTN shares.

² Lpath, Inc. press release, "Lpath Presents Compelling New Preclinical Results of Its Anti-Cancer Drug Candidate, Lpathomab™, at the AACR 100th Annual Meeting." Apr. 20, 2009.

³ Sabbadini, RA. Targeting sphingosine-1-phosphate for cancer therapy. British Journal of Cancer 2006; 95: 1131-35.

CONTENTS

KEY EVENTS AND MILESTONES	5
ABOUT ASONEP™	6
PHASE I STUDY OVERVIEW.....	7
ABOUT ISONEP™	8
PHASE I STUDY OVERVIEW.....	9
POSSIBLE CLINICAL USES OF ISONEP™	10
ABOUT LPATHOMAB™	12
LPA IN HEALTH & DISEASE.....	12
LPATHOMAB™ FOR PULMONARY FIBROSIS.....	14
LPATH'S DRUG DISCOVERY OVERVIEW: IMMUNEY2™	15
INVESTMENT CONCERNS AND RISKS	16
FINANCIAL ANALYSIS.....	17
REVENUE MODEL.....	17
INCOME STATEMENT	22
HISTORICAL BALANCE SHEET	23
DISCOUNTED CASH FLOW (DCF) MODEL.....	24
DISCLOSURES	25

KEY EVENTS AND MILESTONES

- ❑ **2H 2009** – Complete Phase I clinical trial of ASONEP.
- ❑ **2H 2009** – Complete Phase I clinical trial of iSONEP.
- ❑ **1H 2010** – Merck-Serono final decision on option for ASONEP (assuming extension).
- ❑ **2H 2010** – Initiate Phase II clinical trial of ASONEP in RCC and possibly another tumor type as well.
- ❑ **2H 2010** – Initial Phase II clinical trial of iSONEP in wet AMD, with a possible focus on those with occult disease.
- ❑ **FY 2011** – Submit investigational new drug application (IND) for Lpathomab in fibrosis, cancer, and/or ocular disorders.

(Intentionally left blank)

ABOUT ASONEP™

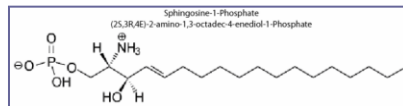
Lpath's product candidate ASONEP (the systemic formulation of sonecipzumab) is an antibody that binds the bioactive lipid sphingosine-1-phosphate (S1P) and thus has promise as a therapy for cancer, multiple sclerosis, and other diseases.

S1P and Cancer

Multiple studies have demonstrated that cancer cells have abnormal levels of sphingolipids and related enzymes involved in the biosynthetic pathway, resulting in conditions that favor cell survival.¹⁰

For instance, ceramide levels of ovarian, lung, and non-squamous head and neck cancers are significantly lower than those found in the corresponding normal tissues (note: ceramide promotes cell death). Other tumors, which include colorectal, breast, uterine, and kidney cancer, express abnormally high sphingosine kinase-1 activity (this kinase converts ceramide into S1P, which resists cell death). Combined, these two situations tilt the sphingolipid rheostat strongly in favor of cell survival, thereby helping malignant cells resist the effects of radiation and chemotherapy.

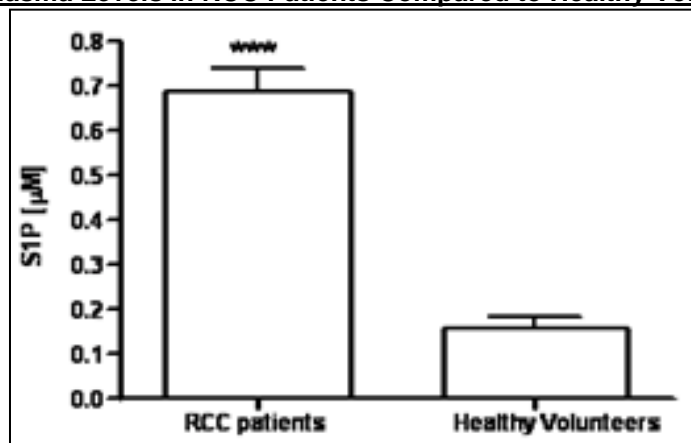
Certain chemotherapeutic agents stimulate *de novo* synthesis of ceramide; among these are daunorubicin, irinotecan, etoposide, and gemcitabine. In contrast, ionizing radiation causes ceramide levels to increase by activating acid sphingomyelinase. This enzyme is also implicated in mediating the apoptotic effects of UVA-light and TNF α . Although different mechanisms are involved, all of these interventions shift the sphingolipid balance toward ceramide-induced apoptosis. Lpath's ASONEP, on the other hand, shifts this balance by neutralizing the S1P.



The rationale behind the development of ASONEP as an oncotherapy is based partly on the antibody's ability to reduce free S1P levels and thereby create conditions that favor apoptosis. This approach makes sense, since erythrocytes and platelets release the sphingolipid to help control thymocyte and lymphocyte tissue distribution.⁴ As a result, S1P, which is often associated with high-density lipoproteins in circulation, is found at concentrations roughly 100 times higher in blood than those recorded in other types of tissue. This means that the largest source of S1P is readily accessible to the antibody ASONEP.

The drug's efficacy as a single agent against different xenograft models lays the groundwork for its use as a standalone therapy. Its dual mechanism of action, tilting the "sphingolipid rheostat" toward apoptosis and inhibiting blood vessel formation, render it a suitable candidate for further studies against solid tumors. The most likely targets include neoplasms that express high sphingosine kinase-1 activity (colorectal, breast, uterine, and kidney) and those that have abnormally low levels of ceramide (ovarian, lung, and non-squamous head and neck). The following graph displays elevated S1P plasma levels in renal cell carcinoma (RCC) (kidney cancer) patients, one potential target for ASONEP, compared to healthy volunteers:

S1P Plasma Levels in RCC Patients Compared to Healthy Volunteers



Source: Lpath, Inc.

⁴ Hanel, P, et al. Erythrocytes store and release sphingosine 1-phosphate in blood. FASEB J 2007; 21: 1202.

Notably, pre-clinical proof-of-principle data in a murine model of RCC presented in April at the 100th Annual Meeting of the American Association for Cancer Research (AACR) demonstrated that ASONEP administered as a single agent delayed the progression of RCC.

The RCC results are presented in the table below:

Time to Progression for Renal Cell Tumors

Drug Product	Number of Days to Grow 2mm	Number of Days to Reach 20mm
Sunitinib (Sutent®)	12.0 +/- 1.16	49.0 +/- 6.7
Anti-S1P (10 mg/kg)	15.3 +/- 3.5	61.7 +/- 15.2
Anti-S1P (50 mg/kg)	20.4 +/- 4.4	63.3 +/- 15.9

Source: Lpath, Inc., James Mier 2009.

These initial results were comparable to the standard of care for the treatment of RCC, VEGF receptor tyrosine kinase inhibitors (TKIs), including the approved TKIs Sutent® and Nexavar®. At higher doses of the anti-S1P agent, the initial results exceeded Sutent®.

The drug may also prove effective in combination with other anticancer agents, given its unique mechanisms of action. Indeed, ASONEP may well act synergistically with established anticancer medicines by rendering the malignant cells susceptible to chemotherapy by shifting the “sphingolipid rheostat” toward apoptosis. Lowering S1P levels or increasing ceramide concentrations in prostate cancer cells increases their sensitivity to radiation and to the chemotherapeutic agents docetaxel and camptothecin.^{5,6} Similar results have been obtained when human lung cancer cells were treated with cisplatin, carboplatin, and doxorubicin, a drug related to Merck-Serono’s UFT® (an oral formulation of 5-fluorouracil)⁷.

PHASE I STUDY OVERVIEW

ASONEP Study Details

Dosing: Dose escalation; intravenous administration of 1.0, 3.0, 10.0 17.0 or 24.0 mg/kg; four or more doses per patient; three patients per cohort.

Primary Endpoint: To determine safety, tolerability, maximum tolerated dose and dose-limiting toxicity of ASONEP.

Phase Ia dose escalation study (15 evaluable patients) showed good tolerability and no drug-related serious adverse events. A Phase Ib extension, where 6 patients (with 3 of them having RCC) are being dosed 24 mg/kg is nearing completion. We expect Lpath to continue to collaborate with academics and others and to hold meetings with Merck-Serono to finalize the Phase II strategy. Given the initial proof-of-principal data in RCC, we expect Lpath to advance ASONEP in a Phase II involving patients with RCC and later to expand its clinical utility to other types of cancer.

⁵ Nava, VE, et al. Sphingosine enhances apoptosis of radiation-resistant prostate cancer cells. *Cancer Res* 2000; 60: 4468.

⁶ Pchejetski, D, et al. Chemosensitizing effects of sphingosine kinase -1 inhibition in prostate cancer cell and animal models. *Mol Cell Therap* 2008; 7: 1836.

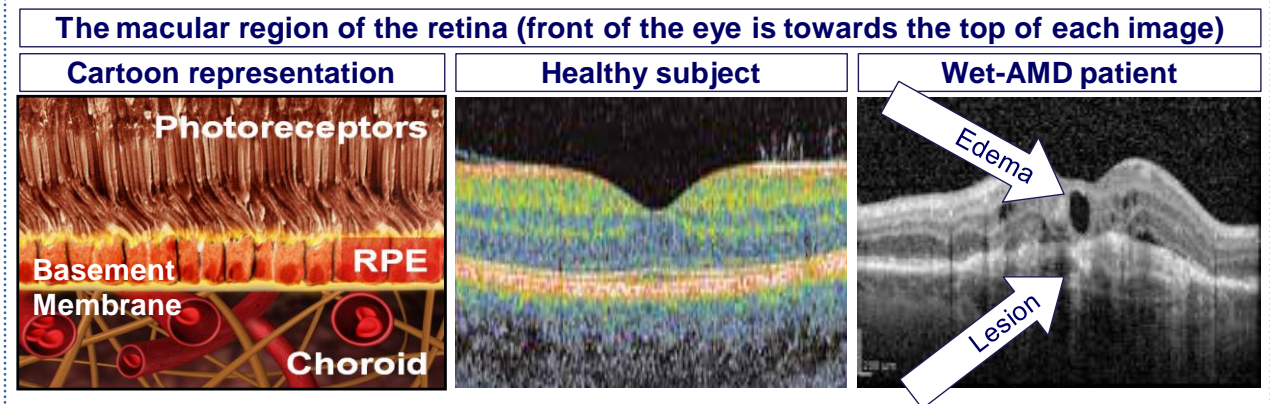
⁷ Min, J, et al. Sphingosine-1-phosphate lyase regulates sensitivity of human cells to select chemotherapy drugs in a p38-dependent manner. *Mol Cancer Res* 2005; 3(5): 287.

ABOUT ISONEP™

iSONEP, the ocular formulation of sonepcizumab, has demonstrated several important mechanisms of action that suggest its usefulness in treating eye diseases; notably, the inhibition of angiogenesis, inflammation (macrophage infiltration), and fibrosis, while also reducing vascular permeability. This combination of actions has considerable promise for a long-term therapy for a host of ocular maladies.

S1P modulates the AMD-associated processes of angiogenesis, inflammation and fibrosis. A potential strategy for treating choroidal neovascularization associated with AMD is to reduce the biologically available extracellular levels of S1P. iSONEP is highly selective for S1P and binds with picomolar affinity. Lpath, in its first wet AMD trial proposes that iSONEP would deprive many cell types (fibroblasts, pericytes, vascular endothelial cells and inflammatory) of important growth and survival factors thus targeting the multiple maladaptive processes of exudative AMD that ultimately result in the loss of photoreceptors, their supporting cells, and visual acuity. Simultaneously targeting multiple components of the choroidal neovascular response is a novel approach and has the potential to be more potent than "single-targeted" therapeutics such as anti-VEGF therapies.⁸

Wet AMD: Neovascular or exudative AMD, the "wet" form of advanced AMD, causes vision loss due to the development of "lesions" created by abnormal blood vessel growth (choroidal neovascularization) in the choriocapillaris, through Bruch's membrane, ultimately leading to blood and protein leakage below the macula. The leakage creates cysts of retinal edema, which can cause the retina to swell and thicken, resulting in loss of vision and visual distortions. AMD begins in the retinal pigment epithelium (RPE), a layer of cells responsible for transporting oxygen and sugars to the retina and removing waste products from the retina. In the case of wet AMD, the RPE cells fail to regulate the growth of blood vessels from the choroid into the retina. In some cases, detachment of the RPE layer can occur as AMD progresses.



Source: Lpath, Inc.

Bleeding, leaking, and scarring from these blood vessels eventually causes irreversible damage to the photoreceptors and rapid vision loss if left untreated. AMD is a leading cause of blindness in adults over 55 years of age. An estimated 15 million people in the United States have age-related macular degeneration (AMD), with more than 1.6 million experiencing the active blood vessel growth and blood vessel leakage associated with wet AMD with the numbers expected to increase as the population ages.

⁸ Clintrials.gov. Safety Study of iSONEP (Sonepcizumab/LT1009) to Treat Neovascular Age-related Macular Degeneration

PHASE I STUDY OVERVIEW

iSONEP Study Details

Dosing: Dose escalation; single intravitreal injection of 0.2, 0.6, 1.0 1.4 or 1.8 mg/eye.

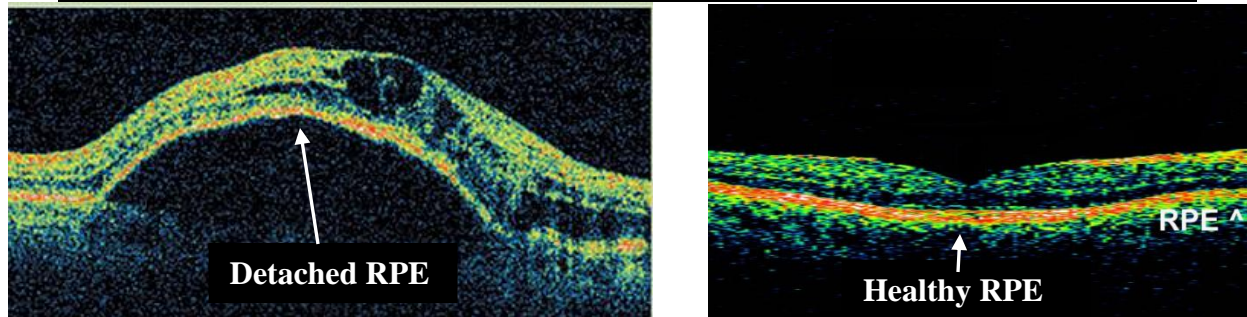
Endpoints:

Primary: To determine safety, tolerability, maximum tolerated dose and dose-limiting toxicity of iSONEP following a single intravitreal injection to subjects with choroidal neovascularization secondary to AMD. Time Frame: Active phase: 30 days post-injection; Follow-up phase: 12 months post-injection.

Secondary: To characterize systemic pharmacokinetics, evaluate the immunogenicity, and investigate preliminary efficacy on retinal lesion thickness determined by OCT; size and extent of CNV and lesion area; and visual acuity. Time Frame: Active phase: 30 days post-injection; Follow-up phase: 12 months post-injection.

Lpath is currently investigating the use of iSONEP against age-related macular degeneration (AMD), a leading cause of severe vision loss. The Phase I clinical trial was recently completed in patients with wet AMD, a condition characterized by pathologic neovascularization under the macula, accompanied by localized blood/serum leakage and inflammatory cell infiltration. Notably, several patients showed a reduction in retinal thickness and regression of lesion size. Significant biological benefit was observed during the 30-40 days following just a single injection in all five of the patients with an “occult choroidal neovascularization (CNV)” present. The average reduction in CNV lesion size was 77% for this group of patients, and, for the two that had retinal pigment epithelium (RPE) detachment, the condition was virtually resolved within 45 days. The RPE is a layer of cells responsible for regulating the transmission of oxygen, sugars, other nutrients, and waste to and from the retina. AMD begins in the RPE layer when the cells fail to regulate the buildup of waste and blood vessel growth from the choroid to the retina. The images below illustrate the difference between a detached and a healthy RPE layer:

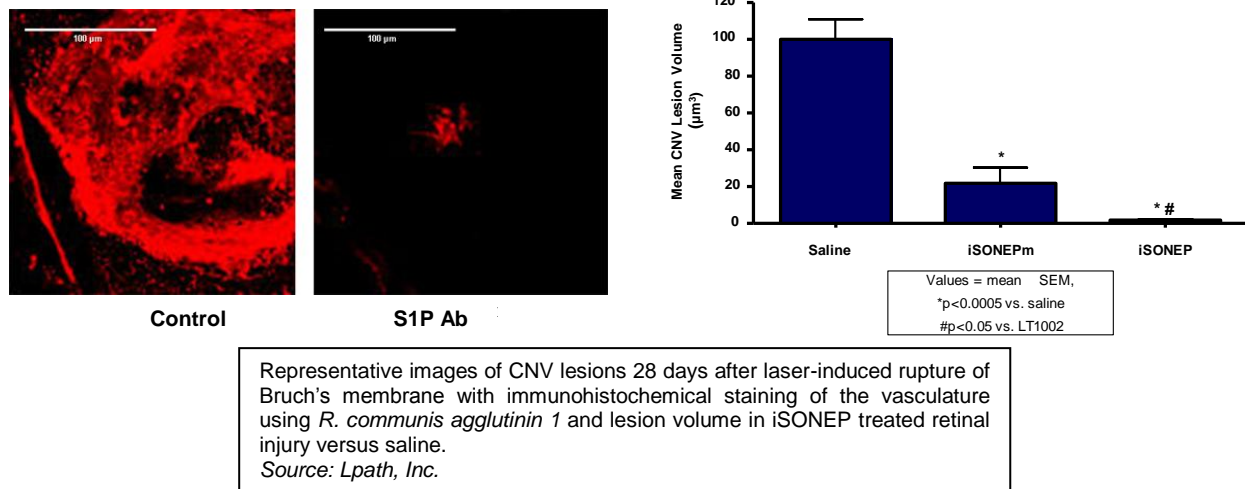
A Comparison between a Detached and a Healthy Retinal Pigment Epithelium (RPE) Layer



Source: Eye 2009

Neither Lucentis® nor Avastin® typically show this type of clinical benefit with a single dose; in fact, in the MARINA Phase 3 trial, Lucentis-treated patients with occult disease experienced an average of 3% reduction in lesion size after 12 monthly injections (vs. 77% average reduction in iSONEP’s Phase I trial). Importantly, from a potential commercial perspective, iSONEP was providing improvement in these patient’s eyes with non-overlapping effect with the VEGF inhibitors (Lucentis and Avastin, and, if approved, the VEGF-Trap). In addition, iSONEP was well tolerated at all dose levels tested and no drug-related serious adverse events were reported.

Previous studies with iSONEP have yielded supporting data to suggest that iSONEP will prove effective in reducing the size of the lesions. In a murine model of retinal injury, it strongly retarded vascular permeability that was created via laser damage to Bruch's membrane (see the image below).⁹



POSSIBLE CLINICAL USES OF iSONEP™

S1P and the Eye

Bioactive lipids, including S1P, are intimately involved in the regulation of various aspects of eye physiology. The two key locations are the cornea and retina.

The Cornea: An important aspect of normal eye physiology is leakage of vitreous humor across the endothelial barrier into the stroma where it provides nutrients to the cells of the stroma and basal epithelium. Normal transfer of fluid and its return are dependent on the integrity of epithelial and endothelial layers, which are subject to regulation by a variety of factors. S1P participates in modulating the endothelial layer's permeability by altering the density of an intracellular cytoskeleton component, F-actin, around the periphery of the cells.¹⁰ This helps to maintain the cells' shape and the junctions between cells, both of which can affect the flow of nutrients into the stroma. In addition, a close chemical relative of S1P, lysophosphatidic acid (LPA), appears to have a similar role in maintaining the tight junctions between epithelial cells. It is found in the aqueous humor and lachrymal gland fluid, and has a role in the healing process whenever the cornea is injured. Indeed, LPA stimulates proliferation of the three major cell types of the cornea (epithelial cells, keratinocytes, and endothelial cells) in response to injury.

The Retina: Bioactive lipids are intimately involved in the biochemical processes that enable cells in the eye to respond to light. Studies^{11,12} have shown that during periods of dark adaptation, LPA and S1P increase the formation of docosahexaenoic acid, the predominant structural fatty acid in the photoreceptors of the retina. Thus, the bioactive lipids support the turnover of membrane components that maintain cell polarity and the delivery of rhodopsin to the photoreceptor. (Rhodopsin is the pigment that is highly sensitive to light and enables night vision.) What's more, there is evidence that the "sphingolipid rheostat" plays a role in vision, for ceramide counters the stimulatory effect of S1P on retinal docosahexaenoic acid formation and promotes apoptosis of the photoreceptors in response to oxidative stress.¹³

⁹ Stoller, G, et al. A novel humanized monoclonal antibody against the bioactive lipid sphingosine-1-phosphate strongly inhibits choroidal neovascularization (CNV) in a murine model. Presented at the 2007 ARVO Annual Meeting (May, 2007).

¹⁰ McVerry, BJ, and Garcia GN. Endothelial cell barrier regulation by sphingosine 1-phosphate. *J Cell Biol* 2004; 92: 1075.

¹¹ Deretic, D, et al. Phosphoinositides, ezrin/moesin, and rac1 regulate fusion of rhodopsin transport carriers in retinal photoreceptors. *Mol Biol Cell* 2004; 15: 359.

¹² Pasquare, SJ, et al. Involvement of lysophosphatidic acid, sphingosine 1-phosphate and ceramide 1-phosphate in the metabolism of phosphatidic acid by lipid phosphate phosphatases in bovine rod outer segments. *Neurochem Res*, doi: 10.1007/s11064-007-9569-5 (Epub ahead of print Feb 2, 2008).

¹³ German, OL, et al. Ceramide is a mediator of apoptosis in retina photoreceptors. *Invest Ophthalmol Vis Sci* 2006; 47(4): 1658.

Given the multiple levels at which S1P modulates eye function, iSONEP could prove useful in a variety of ocular disorders, including (i) age-related macular degeneration (AMD), (ii) diabetic retinopathy, (iii) scarring caused by retinal surgery, and (iv) proliferative vitreoretinopathy (PVR).

Lpath is currently investigating the use of iSONEP against age-related macular degeneration (AMD), a leading cause of severe vision loss. A Phase I clinical trial was recently completed in patients with wet AMD, a condition characterized by pathologic neovascularization under the macula, accompanied by localized blood/serum leakage and inflammatory cell infiltration. Current treatments for wet AMD, which include pegaptanib (sold as Macugen® by **OSI Pharmaceuticals, Inc. (NASDAQ:OSIP)/Pfizer, Inc. (NYSE:PFE)**) and ranibizumab (sold as Lucentis® by **Genentech, Inc. (NYSE:DNA)**), attempt to suppress angiogenesis by blocking the biological activity of VEGF. This approach falls short of providing optimal therapy, however, since recent studies (ANCHOR and MARINA trials) found that a majority of patients (60%) treated with Lucentis® did not experience visual gain, and those who had a successful response did not regain visual acuity.^{14,15} Thus, novel therapeutic modalities for wet AMD are needed, and iSONEP offers an attractive candidate, in our view. In fact, in the completed Phase I trial, several patients showed a reduction in retinal thickness and regression of lesion size. Most of the patient's lesions were challenging from a treatment perspective, and iSONEP provided improvement in these patient's eyes with non-overlapping effect with the other treatments. Lpath's drug candidate directly blocks S1P-induced endothelial cell migration/infiltration and blood vessel formation, and indirectly inhibits angiogenesis mediated by three different growth factors, platelet-derived growth factor, bFGF and VEGF. As such, we believe Lpath will probably pursue a protocol featuring iSONEP in combination with Lucentis® for a Phase II clinical trial.

iSONEP's broad spectrum of biological activity may also render it useful against diabetic retinopathy, the leading cause of blindness in the United States. Like wet AMD, this disease is characterized by abnormal blood vessels in the retina, followed by loss of vascular integrity and increased permeability. Currently, patients are treated with scatter laser therapy, which helps to shrink the abnormal blood vessels before they begin to leak blood/plasma into the vitreous humor. Moreover, experimental data found that anti-S1P was more effective than an anti-VEGF medicine (VEGF-Trap) in inhibiting blood vessel formation and leakage.^{16,17} (VEGF-Trap consists of two recognition sites from the VEGF receptor that act by binding the growth factor, much like an antibody would. This bioengineered molecule was created by **Regeneron (NASDAQ:REGN)**, but Bayer currently has a worldwide license to the drug for ocular applications.)

Wet AMD Combination treatment protocol. The current treatment protocols for wet AMD utilize a combination of two, or even three, modalities delivered simultaneously to minimize re-treatments and optimize gain in visual acuity. Intravitreal anti-VEGF agents have been combined with intravitreal steroids) and, in some cases, in combination with PhotoDynamic Therapy (PDT). iSONEP™'s multiple anti-inflammatory, anti-fibrotic and anti-angiogenic properties could be a favorable in a combination therapy that may reduce the need for re-treatment.

Lpath is also developing iSONEP to exploit its anti-fibrotic activity. A preclinical study¹⁸ has already provided evidence of the involvement of S1P in a fibrotic disorder, proliferative vitreoretinopathy. This condition, which is the most common cause of failure in retinal detachment surgery, is characterized by an aberrant reparative process that involves macrophage infiltration, collagen deposition, and the transformation of normal retinal pigmented epithelial cells into fibrocontractile, myofibroblast-like cells expressing muscle actin-containing fibers. Research has shown that S1P promotes collagen production by myofibroblasts and that, as in the lung, TGFβ has shown profound profibrotic activity, possibly through the action of S1P.¹⁹ This suggests that iSONEP could mitigate the pro-fibrotic effects of TGFβ and the

¹⁴ Rosenfeld, PJ, et al. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006; 355: 1419.

¹⁵ Brown, DM, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *N Engl J Med* 2006; 355: 1432.

¹⁶ Saishin, Y, et al. VEGF-TRAP_{R1R2} suppresses choroidal neovascularization and VEGF-induced breakdown of the blood-retinal barrier. *J Cell Physiol* 2003; 195(2): 241.

¹⁷ Lpath, Inc. Company Presentation at BIO-CEO Conference in New York City (February, 2007).

¹⁸ Swaney, J, et al. Sphingosine-1-phosphate is a novel lysolipid mediator of epithelial-to-mesenchymal transition by human retinal pigmented epithelial (RPE) cells. Presented at the 2007 ARVO annual meeting (May, 2007).

¹⁹ Squires, CE, et al. Altered fibroblast function following myocardial infarction. *J Mol Cell Cardiol* 2005; 39(4): 699.

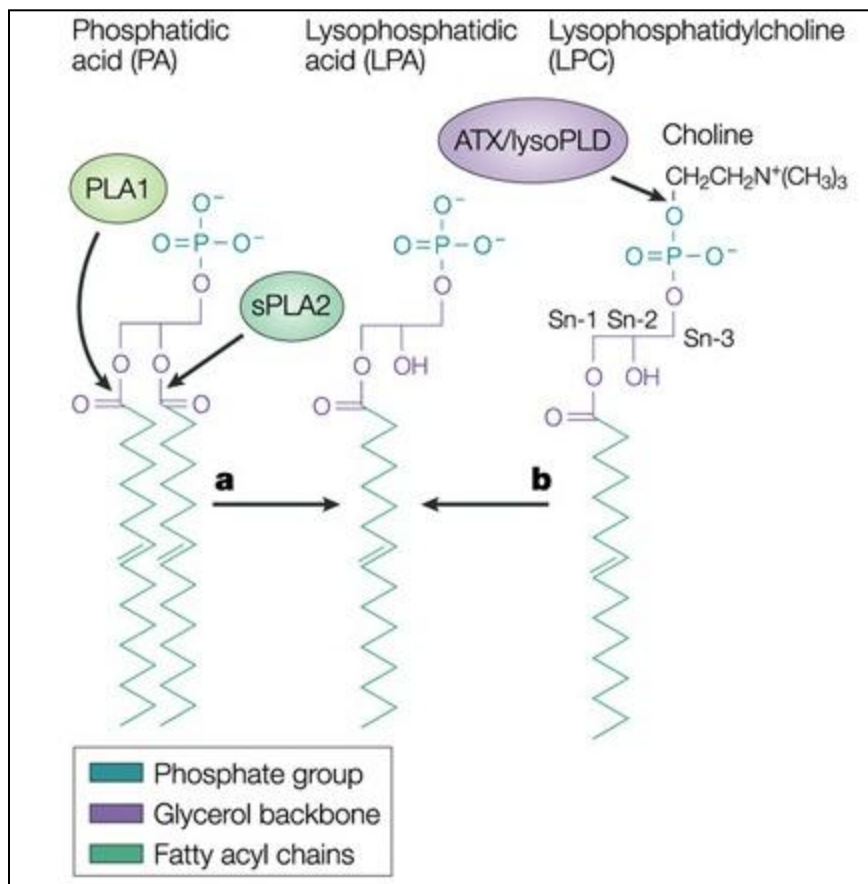
fibrogenic effects of S1P itself. An antibody against S1P markedly limited collagen deposition in the subretinal area following laser rupture of Bruch's membrane.

ABOUT LPATHOMAB™

Lpathomab, Lpath's third mAb-based drug candidate, targets the bioactive lipid lysophosphatidic acid (LPA). This therapeutic agent is at a somewhat earlier stage of development than its S1P-targeted counterparts, but the Company's efforts to scale up manufacturing of the antibody and to prepare an IND filing warrant its inclusion in our financial model. Lpathomab has shown anti-fibrotic and anti-angiogenic activity, as well as anti-metastatic and anti-tumorigenic activity. In other words, it is an attractive drug candidate for a wide range of diseases. Lpath has successfully humanized Lpathomab and will soon choose its lead indication in preparation for IND-enabling studies. The Company plans to file one or more Investigational New Drug applications (INDs) for Lpathomab in 2011.

LPA IN HEALTH & DISEASE

Like S1P, LPA is synthesized and released by platelets into the serum to help regulate several cellular processes including platelet aggregation, cytoskeleton remodeling, and cell proliferation, survival and migration. It also shares the anti-apoptotic properties of S1P. Two principle enzymes contribute to its production, as shown below:^{20,21}



Biosynthetic pathways of lysophosphatidic acid (LPA). Two types of enzymes have been identified in the phospholipid's synthesis: phospholipase A (PLA1 and sPLA2, or secretory phospholipase A2), and ATX/lysoPLD, which is known as both autotaxin and phospholipase D.⁴⁰

Of the enzymes that produce LPA, phospholipase D is considered the most important source of the phospholipid in blood. This enzyme, which is also known as autotaxin, is a secreted enzyme that synthesizes the phospholipid extracellularly after its substrates are released from activated platelets (in response to injury, inflammation, or atherosclerosis), adipocytes, and many different cancer cells. This

²⁰ Mills, GB, and Moolenaar, WH. The emerging role of lysophosphatidic acid in cancer. *Nature Reviews Cancer* 2003; 3: 582.

²¹ Aoki, J, et al. Serum lysophosphatidic acid is produced through diverse phospholipase pathways. *J Biol Chem* 2002; 277(50): 48737.

enzyme is essential for blood vessel formation during embryogenesis and it appears to play a part in the development of obesity-associated diabetes.^{22,23} The physiological roles of the phospholipase A family of enzymes have not been fully defined, though at least some of the forms are involved in prostaglandin synthesis in various cells, including lung fibroblasts.²⁴ They also appear to participate in such pathological conditions as psoriasis and cancers of the testis, skin, and ovaries.^{25,26,27,28}

LPA exerts its influence through the activation of G-protein coupled receptors (GPCRs) that belong to one of two families. One group, comprised of the LPA₁, LPA₂, and LPA₃ receptors, has 50%-57% homologous amino acid sequences and is associated with a single G protein that propagates the messages intracellularly. The other family is not related to the first group structurally, and is coupled to several different G proteins. The six receptors differ in the levels of their expression and the tissues in which they are found. Nonetheless, virtually all mammalian cells and organs express multiple LPA receptor types. This appears to permit fine control over some cellular processes regulated by LPA (e.g., cell motility), and it allows LPA to influence some processes in the same cell via different pathways (e.g., anti-apoptosis).^{29,30}

Given the general cellular functions that LPA influences and the variety of receptors, it is not surprising that it has a wide range of activity. For instance, this bioactive lipid plays a role during conception by affecting implantation of the fertilized egg and subsequently directs the differentiation of certain neural stem cells into oligodendrocytes. (These cells become the insulation that is required for proper signal transduction along nerve fibers via a process called myelination.)^{31,32} LPA also facilitates wound healing through its effects on fibroblasts, endothelial cells, and smooth muscle cells. This activity is not limited to the skin, but takes place in such distinct areas as the lungs, eyes, and brain. Typically, it participates in pathways that attract fibroblasts from the bloodstream to a site of injury and that promote local myofibroblast formation, which leads to the deposition of extracellular matrix and tissue remodeling.³³ This process involves the opening of chloride ion channels in fibroblasts or their equivalent (e.g., keratocytes in the eye), resulting in a chloride ion flow that is essential for transforming growth factor- β (TGF- β) induced differentiation of fibroblasts into myofibroblasts.^{34,35} (TGF- β is considered the most important signal involved in fibrosis.)

LPA has also been implicated in various pathological conditions, notably various cancers in which the malignant cells express aberrant levels of LPA and/or its receptors. This bioactive lipid is found at elevated levels in ovary, kidney, breast, and brain cancers. Moreover, expression of its receptors appears to follow a pattern in various cancers, including ovarian colorectal, prostate, and breast.^{36,37} In each case,

²² Ferry, G, et al. Functional invalidation of the autotaxin gene by a single amino acid mutation in mouse is lethal. *FEBS Lett* 2007; 581(18): 3572.

²³ Boucher, J, et al. Potential involvement of adipocyte insulin resistance in obesity-associated up-regulation of adipocyte lysophospholipase D/autotaxin expression. *Diabetologia* 2005; 48: 569.

²⁴ Ghosh, M, et al. Function, activity, and membrane targeting of cytosolic phospholipase A₂ ζ in mouse lung fibroblasts. *J Biol Chem* 2007; 282(16): 11676.

²⁵ Foell, JL, et al. Membrane-associated phospholipase A1 beta (LIPI) is an Ewing tumour-associated cancer/testis antigen. *Pediatr Blood Cancer* 2008; 51(2): 228.

²⁶ Nagai, Y, et al. An alternative splicing form of phosphatidylserine-specific phospholipase A1 that exhibits lysophosphatidylserine-specific lysophospholipase activity in humans. *J Biol Chem* 1999; 274(16): 11053.

²⁷ Ren, J, et al. Lysophosphatidic acid is constitutively produced by human peritoneal mesothelial cells and enhances adhesion, migration, and invasion of ovarian cancer cells. *Cancer Res* 2006; 66(6): 3006.

²⁸ Chiba, H, et al. Cloning of a gene for a novel epithelium-specific cytosolic phospholipase A2, cPLA2delta, induced in psoriatic skin. *J Biol Chem* 2004; 279(13): 12890.

²⁹ Lee, Z, et al. Role of LPA₄/p2y9/GPR23 in negative regulation of cell motility. *Mol Biol Cell* pre-publication, posted October 8, 2008.

³⁰ Lin, FT, et al. The lysophosphatidic acid 2 receptor mediates down-regulation of Siva-1 to promote cell survival. *J Biol Chem* 2007; 282(52): 37759.

³¹ Liszewska, E, et al. Lysophosphatidic acid signaling during embryo development in sheep: involvement in prostaglandin synthesis. *Endocrinol* pre-publication, posted September 4, 2008.

³² Hui-Lin, C and Jian-Tian, Q. Effect of lysophosphatidic acid on differentiation of embryonic neural stem cells into neuroglial cells in rates *in vitro*. *Acta Physiol Sinica* 2007; 59(6): 759.

³³ Wang, J, et al. Receptor-mediated activation of a Cl⁻ current by LPA and S1P in cultured corneal keratocytes. *Invest Ophthalmol Vis Sci* 2008; 43(10): 3202.

³⁴ Yin, Z and MA Watsky. Chloride channel activity in human lung fibroblasts and myofibroblasts. *Am J Physiol Lung Cell Mol Physiol* 2005; 288(6): L1110.

³⁵ Wang, J, et al. Receptor-mediated activation of a Cl⁻ current by LPA and S1P in cultured corneal keratocytes. *Invest Ophthalmol Vis Sci* 2008; 43(10): 3202.

³⁶ Shida, D, et al. Aberrant expression of lysophosphatidic acid (LPA) receptors in human colorectal cancer. *Lab Invest* 2004; 84: 1352.

LPA₂ receptors are found in excess, while LPA₁ receptors decline and LPA₃ levels remain at a low level. Work performed with several ovarian cancer cell lines has further demonstrated that LPA stimulates tumor growth directly by boosting synthesis of the interleukins 6 and 8,³⁸ as well as cyclin D1,³⁹ a member of a family of three proteins that regulate the cell cycle. The bioactive lipid also promotes tumor growth indirectly via stimulation of VEGF production and therefore blood vessel formation.⁴⁰

LPA plays a role in other diseases based on the various normal cellular processes in which it is involved. For instance, it has been implicated in the development of neuropathic pain, based on its ability to initiate a key characteristic of the disease, aberrant nerve demyelination.⁴¹ And it plays a role in the deposition of abnormal fibrotic tissue in such tissues/organs as the kidneys, liver, lungs, and skin.

LPATHOMAB™ FOR PULMONARY FIBROSIS

Based partly on this antibody's ability to interfere with scar formation, there are a number of potential applications, but one of the most compelling from a clinical standpoint involves conditions that fall into the general category of interstitial lung diseases. This group of chronic lung disorders is characterized by three traits: (1) the lung is damaged via a known or unknown mechanism; (2) inflammation (not necessarily overt) develops in the walls of the air sacs; and (3) scar tissue forms in the interstitium, the tissue between the air sacs. As a result of this cyclical process, the lung progressively loses its pliability and capacity to adequately oxygenate the body, particularly during physical exertion. Some progress has been made in treating pulmonary fibrosis with anti-inflammatory, cytotoxic, and antifibrotic drugs, but halting disease progression remains an unmet need. Indeed, patients who are diagnosed with the most common interstitial lung disease, idiopathic pulmonary fibrosis, face a life expectancy of only 2 to 5 years.

The etiologies of the different conditions comprising interstitial lung diseases differ, but they ultimately result in abnormal deposition of extracellular matrix and increased vascularization of the lung. Patients at greatest risk of developing one of these diseases have increased numbers of myofibroblasts, which are activated fibroblasts that express certain traits akin to smooth muscle cells and normally play a role in wound healing by contracting the edges of the wound. Their persistent presence is believed to be important to lung pathology, since they produce extracellular matrix, including collagen, and exhibit contractile properties involved in tissue remodeling. The molecular mechanisms underlying disease development and progression are not fully known, although LPA has been strongly implicated in tissue remodeling, fibrosis, and inflammation.

LPA's role in pulmonary fibrosis is partly related to its direct effects on fibroblasts. A recent study has shown that this bioactive lipid results in coordinated transcriptions of specific genes in several temporally distinct phases that begin about 30 minutes after exposure and end about 24 hours later.⁴² The initial genes expressed directly alter the cell cycle via both positive and negative regulators of cycle progression. Other genes that are upregulated include proteins of the cytoskeleton, which control the cell's shape and motility, and extracellular matrix proteins that support cell attachment and migration. LPA also induces signalling molecules (i.e., mitogens, chemokines, and pro-angiogenic factors) that underpin the inflammatory process. LPA also enhances contractility of airway smooth muscle and acts synergistically with epidermal growth factor (EGF) in stimulating mitogenesis of these cells. (This is at least partly attributable to an induction of EGF receptors by LPA.) Like fibroblasts, epithelial cells respond to LPA by increasing the expression of multiple transcription factors, causing the extension of filopodia and the secretion of fibronectin⁴³. Thus, the bioactive lipid supports the transition of epithelial cells to mesenchymal cells with a myofibroblast phenotype. This cellular conversion, which is promoted by TGF-

³⁷ Kitayama, J, et al. Over-expression of lysophosphatidic acid receptor-2 in human invasive ductal carcinoma. *Breast Cancer Res* 2004; 6: R640.

³⁸ Fang, X, et al. Mechanisms for lysophosphatidic acid-induced cytokine production in ovarian cancer cells. *J Biol Chem* 2004; 279(10): 9653.

³⁹ Hu, YL, et al. Dual mechanisms for lysophosphatidic acid stimulation of human ovarian carcinoma cells. *J Natl Cancer Inst* 2003; 95(10): 733.

⁴⁰ Hu, YL, et al. Lysophosphatidic acid induction of vascular endothelial growth factor expression in human ovarian cancer cells. *J Natl Cancer Inst* 2001; 93(10): 762.

⁴¹ Ueda, H. Peripheral mechanisms of neuropathic pain – involvement of lysophosphatidic acid receptor-mediated demyelination. *Mol Pain* 2008; 4: 11.

⁴² Stortelers, C, et al. Multiple actions of lysophosphatidic acid on fibroblasts revealed by transcriptional profiling. *BMC Genomics* 2008; 9: 387.

⁴³ Toews, M> et al. Lysophosphatidic acid in airway function and disease. *Biochim biophys Acta* 2002; 1582(1-3): 240.

$\beta 1$ (the key growth factor in fibrosis), is crucial to lung remodeling associated with disease.⁴⁴ Research using a gene knock-out model has lent support to LPA's involvement in pulmonary fibrosis by showing that the LPA₁ receptor is required for the recruitment of fibroblasts and the development of leaky blood vessels in the lung in response to an experimental insult.⁴⁵

Preclinical studies with Lpathomab have shown that the drug exhibits antifibrotic activity in bleomycine-induced pulmonary fibrosis, and work is under way to secure FDA approval to initiate at least one clinical trial in 2011.⁴⁶

Given the strong evidence of LPA's involvement in abnormal fibrosis, we believe Lpath will select a serious fibrotic disease for commercializing of Lpathomab. Our financial model is based on an assumption that the disease is pulmonary fibrosis, a progressive disease that is lethal. Moreover, we have assumed that the Company develops this drug through a Phase II trial in order to secure a higher royalty rate in a partnering agreement. Considering the other uses for Lpathomab, we believe that iSONEP, like ASONEP, has blockbuster potential.

LPATH'S DRUG DISCOVERY OVERVIEW: IMMUNEY2™

Lpath's ImmuneY2 technology, which consists of a series of proprietary processes, is a drug-discovery engine that provides Lpath the capability of generating a pipeline of novel mAb-based drug candidates against bioactive lipid targets in the emerging lipidomics field. This powerful platform involves (i) a unique methodology of presenting the selected lipid target to the mouse immune system to elicit antibodies against the lipid target (lipids are so small that they do not normally trigger an immune response) and (ii) several proprietary assays that measure the immune response and analyze the performance characteristics of antibodies produced by isolated B lymphocyte cell lines.

To date, no other firm has been able to generate therapeutic mAbs against bioactive lipids, making Lpath the leader in this new and emerging category of drug discovery.

In summary, Lpath's first mAb, sonopczumab, binds sphingosine-1-phosphate, a validated lipid target for multiple diseases, including cancer, AMD, various other ocular disorders, and certain inflammatory, cardiovascular, and fibrotic diseases. The next mAb created, Lpathomab, targets lysophosphatidic acid, a validated target for multiple cancers, various fibrotic diseases, and ocular disorders. What's more, Lpath is using the ImmuneY2 platform to generate additional mAbs against undisclosed lipid targets that should provide an ever-growing pipeline of novel, mAb-based drug candidates.⁴⁷

⁴⁴ Kasai, H, et al. TGF-beta1 induces human alveolar epithelial to mesenchymal cell transition (EMT). *Respir Res* 2005; 6: 56.

⁴⁵ Tager, AM, et al. The lysophosphatidic acid receptor LPA1 links pulmonary fibrosis to lung injury by mediating fibroblast recruitment and vascular leak. *Nat Med* 2008; 14(1): 45.

⁴⁶ Lpath 10K for the year ended December 31, 2007.

⁴⁷ Lpath, Inc. press release, "Lpath Creates First Neutralizing Monoclonal Antibodies Against LPA, an Important Cancer Target: Breakthrough Further Validates Lpath's ImmuneY2™ Process", July 17, 2006.

INVESTMENT CONCERNS AND RISKS

For a complete description of risks and uncertainties related to Lpath, Inc.'s business, see the "Risk Factors" section in Lpath's SEC filings, which can be accessed directly from the SEC Edgar filings at www.sec.gov. Potential risks include:

- ❑ **Stock risk and market risk:** There is a limited trading market for the Company's common stock. There can be no assurance that an active and liquid trading market will develop or, if developed, that it will be sustained, which could limit one's ability to buy or sell the Company's common stock at a desired price. Investors should also consider technical risks common to many small-cap or micro-cap stock investments, such as small float, risk of dilution, dependence upon key personnel, and the strength of competitors that may be larger and better capitalized.
- ❑ **New and rapidly changing field:** The pharmaceutical and biotechnological markets are rapidly evolving, and research and development are expected to continue at an accelerated pace with increased frequency. Other companies are also actively engaged in the development of therapies to directly or indirectly treat those disorders being pursued by Lpath. These companies may have substantially greater research and development capabilities, as well as significantly greater marketing, financial, and human resources abilities than Lpath.
- ❑ **Products still in development phases:** Although the Company intends to continue with clinical development of ASONEP for cancer, iSONEP for wet age-related macular degeneration, and other pipeline candidates in various indications, the successful development of the Company's product candidates is uncertain. Product development costs and timelines can vary significantly for each product candidate and are difficult to accurately predict. Products in development that appear to be promising may not reach commercialization for various reasons, including failure to achieve regulatory approvals, safety concerns, and/or the inability to be manufactured at a reasonable cost. In addition, partners such as Merck Serono may or may not option the Company's clinical development programs, including ASONEP, which could affect the Company's developmental capabilities.
- ❑ **Funding requirements:** It is difficult to predict the Company's future capital requirements. The Company may need additional financing to continue funding the research and development of its products and to expand its business. There is no guarantee that it can secure the desired future capital or, if sufficient capital is secured, that current shareholders will not suffer significant dilution.
- ❑ **Regulatory risk:** Various statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of each product. The lengthy process of seeking approval and the subsequent compliance with applicable statutes and regulations require the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals could materially adversely affect Lpath's business. There is no guarantee that Lpath's products will be approved by the U.S. Food and Drug Administration (FDA) or international regulatory bodies for marketing in the U.S. or abroad.
- ❑ **The Company may need to raise additional capital, which may not be available on terms acceptable to them, if at all:** As the Company continues to expand its research and development and sales and marketing activities, they may need to raise additional capital, which may not be available on terms acceptable to them, if at all. If the Company cannot raise necessary additional capital on acceptable terms, they may not be able to increase sales, develop or enhance their products and services, take advantage of future opportunities, or respond to competitive pressures or unanticipated requirements, any of which could cause their business to suffer.
- ❑ **Competitive risk:** The biotechnology industry is extremely competitive, mainly due to its large market potential. Many companies are developing products for the same therapeutic indications targeted by Lpath. These companies may have substantially more resources than Lpath, which could adversely affect the Company's position in the market place.

FINANCIAL ANALYSIS

REVENUE MODEL

Our revenue model includes iSONEP for wet age-related macular degeneration (AMD) and ASONEP for three indications that we believe are representative of its commercial potential: renal cell carcinoma (RCC), colorectal cancer, and ovarian cancer. In addition, we have included Lpathomab for idiopathic pulmonary fibrosis (IPF). We also expect Lpathomab to be advanced in other types of fibrosis, oncology, and neuropathic pain indications, but we have excluded potential revenue from our model at this time. We believe these opportunities add significant upside potential to our estimates.

Pursuant to the collaboration with Merck Serono, we assume that Lpath will receive (i) an average annual royalty of 9% of total product sales in each approved indication for ASONEP and (ii) total milestone exceeding \$230 million over the life of the product.

We also assume that Lpath will seek marketing partners for (i) iSONEP in exchange for royalties of 15% of total product sales and an upfront fee and milestones totaling \$200 million and (ii) Lpathomab in exchange for royalties of 10% and an upfront fee and milestones totaling \$400 million.

Lastly, we assume that all milestone payments are amortized equally over five years.

iSONEP™: AMD

Year penetration starts	2015	Incidence	2233493
Starting penetration rate	5%	Percent addressable	80%
Years between penetration start and peak	8	Market growth rate	5%
Peak penetration	25%	Annual price per patient	\$3,000
Duration of peak penetration in years	4	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	15%
Stage of development	Phase I	Probability of commercialization	20%

Assumptions:

- ❑ The patient population in 2009 consists of an estimated 2.23 million patients, a number that is increasing faster than the U.S. population due to the aging Baby Boom generation.⁴⁸
- ❑ The percent of the market that is addressable is estimated to be 80%, reflecting the severity of some patients' disease and the inability to reach certain geographic markets.
- ❑ The initial penetration rate is 5%, due to the availability of drugs for wet AMD today and the gradual rollout of iSONEP in the various markets around the world.
- ❑ The peak penetration rate is 25%, reflecting a good level of efficacy, particularly with respect to today's medications.
- ❑ Lpath signs a licensing deal for iSONEP that grants marketing rights to a company experienced in the ophthalmology sector in exchange for royalties of 15%. The deal includes an upfront fee and milestone payments totaling \$200 million.

⁴⁸ The Eye Diseases Prevalence Research Group. "Prevalence of age-related macular degeneration in the United States" Arch Ophthalmol 2004; 122(4): 564. Estimated prevalence of AMD in 2004 was 1.75 million. We assume a 5% annual growth rate.

ASONEP™: Renal Cell Carcinoma - U.S.

Year penetration starts	2015	Incidence	49096
Starting penetration rate	5%	Percent addressable	30%
Years between penetration start and peak	4	Market growth rate	2%
Peak penetration	20%	Price per patient	\$50,000
Duration of peak penetration in years	4	Treatment price growth	1%
Retention rate in decline years	90%	Royalty rate	9%
Stage of development	Phase I	Probability of commercialization	20%

ASONEP™: Renal Cell Carcinoma - ROW

Year penetration starts	2016	Incidence	139871
Starting penetration rate	5%	Percent addressable	30%
Years between penetration start and peak	4	Market growth rate	2%
Peak penetration	15%	Price per patient	\$40,000
Duration of peak penetration in years	4	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	9%
Stage of development	Phase I	Probability of commercialization	20%

Assumptions:

- ❑ The National Cancer Institute (NCI) estimates that there will be approximately 49,096 patients diagnosed with renal cell carcinoma in the United States in 2009, and the International Agency for Research of Cancer (IARC) estimates that there will be approximately 139,871 patients diagnosed in foreign developed countries of the world.^{49,50}
- ❑ Only 30% of the patient population is eligible for ASONEP therapy, since about 60% are diagnosed with Stage I or Stage II disease and are treated surgically. A proportion of the remainder is probably ineligible for drug therapy based on their overall health.
- ❑ Commercialization begins in 2015 with an initial penetration rate of 5% in the United States and in 2016 in foreign markets with an initial penetration rate of 5%.
- ❑ The peak penetration rates are 20% and 15% for the United States and overseas markets, respectively, reflecting a good efficacy rate, but allowing for the potential entrance of other new therapies into the market.
- ❑ The price of therapy is \$50,000 per patient per year in the United States, which is comparable to other monoclonal antibody-based anticancer drugs (e.g. **Genentech's** Avastin).
- ❑ The price of the drug is lower in foreign countries than in the United States, primarily because of differences in pricing policies.
- ❑ We've assumed that the royalty rate averages 9% over the span of the Merck Serono licensing agreement.

⁴⁹ National Cancer Institutes website: "Kidney Cancer," <http://www.cancer.gov/cancertopics/types/kidney>.

⁵⁰ International Agency for Research of Cancer, The Globocan 2002 Database. <http://www-dep.iarc.fr/globocan/database.htm>.

ASONEP™: Colorectal - U.S.

Year penetration starts	2015	Incidence	148810
Starting penetration rate	5%	Percent addressable	60%
Years between penetration start and peak	4	Market growth rate	0%
Peak penetration	20%	Price per patient	\$50,000
Duration of peak penetration in years	4	Treatment price growth	1%
Retention rate in decline years	90%	Royalty rate	9%
Stage of development	Phase I	Probability of commercialization	20%

ASONEP™: Colorectal - ROW

Year penetration starts	2016	Incidence	574600
Starting penetration rate	5%	Percent addressable	60%
Years between penetration start and peak	4	Market growth rate	0%
Peak penetration	15%	Price per patient	\$40,000
Duration of peak penetration in years	4	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	9%
Stage of development	Phase I	Probability of commercialization	20%

Assumptions:

- ❑ The American Cancer Society estimates that there were approximately 148,810 patients diagnosed with colorectal cancer in the United States in 2008, and approximately 574,600 patients diagnosed in foreign developed countries of the world.^{51,52}
- ❑ Only 60% of the patient population is eligible for ASONEP therapy, since about 25% are diagnosed with Stage I disease and are treated surgically. A proportion of the remainder is probably ineligible for drug therapy based on their overall health.
- ❑ Commercialization begins in 2015 with an initial penetration rate of 5% in the United States and in 2016 in foreign markets with an initial penetration rate of 5%.
- ❑ The peak penetration rates are 20% and 15% for the United States and overseas markets, respectively, reflecting a good efficacy rate, but allowing for the potential entrance of other new therapies into the market.
- ❑ The price of therapy is \$50,000 per patient per year in the United States, which is comparable to other monoclonal antibody-based anticancer drugs (e.g. **Genentech's** Avastin).
- ❑ The price of the drug is lower in foreign countries than in the United States, primarily because of differences in pricing policies.
- ❑ We've assumed that the royalty rate averages 9% over the span of the Merck Serono licensing agreement.

⁵¹ Cancer Facts & Figures 2008, published by the American Cancer Society.

⁵² Global Cancer Facts & Figures 2007, published by the American Cancer Society.

ASONEP™: Ovarian - U.S.

Year penetration starts	2015	Incidence	21650
Starting penetration rate	5%	Percent addressable	65%
Years between penetration start and peak	4	Market growth rate	1%
Peak penetration	20%	Price per patient	\$50,000
Duration of peak penetration in years	4	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	9%
Stage of development	Phase I	Probability of commercialization	20%

ASONEP™: Ovarian - ROW

Year penetration starts	2016	Incidence	81700
Starting penetration rate	5%	Percent addressable	65%
Years between penetration start and peak	4	Market growth rate	1%
Peak penetration	15%	Price per patient	\$40,000
Duration of peak penetration in years	4	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	9%
Stage of development	Phase I	Probability of commercialization	20%

Assumptions:

- ❑ The market consists of 21,650 patients who the American Cancer Society estimates will be diagnosed this year with ovarian cancer in the United States and an estimated 81,700 patients in foreign developed countries.^{53,54}
- ❑ The addressable market is 65%, partly because we've assumed that the drug is not approved initially for treatment of patients at an early stage of the disease (e.g. maintenance therapy and as adjuvant therapy with radiation or surgery). On the other hand, approximately 70% of the patients present with advanced cancer, which is commonly treated with chemotherapy. We've assumed that some patients will not be treated with ASONEP™ due to age and general health.
- ❑ Commercialization begins in the United States in 2015 with an initial penetration rate of 5% and in 2016 in foreign markets with an initial penetration rate of 5%.
- ❑ The peak penetration rates are 20% and 15% for the United States and overseas markets, respectively, reflecting a good efficacy rate, but allowing for the potential entrance of other new therapies into the market.
- ❑ The price of therapy is \$50,000 per patient per year in the United States, which is comparable to other monoclonal antibody-based anticancer drugs (e.g. **Genentech's** Avastin), and \$30,000 overseas primarily due to differences in pricing policies.
- ❑ The licensing deal provides an average royalty rate of 9%.

⁵³ Cancer Facts & Figures 2008, published by the American Cancer Society.

⁵⁴ Global Cancer Facts & Figures 2007, published by the American Cancer Society.

Lpathomab™: Idiopathic Pulmonary Fibrosis (IPF)

Year penetration starts	2017	Incidence	520000
Starting penetration rate	5%	Percent addressable	80%
Years between penetration start and peak	4	Market growth rate	1%
Peak penetration	20%	Price per patient	\$40,000
Duration of peak penetration in years	8	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	10%
Stage of development	Phase I	Probability of commercialization	20%

Assumptions:

- ❑ The estimated patient population reflects prevalence of the disease in the United States,⁵⁵ applied to the population of “developed countries” as defined by the U.S. Census Bureau.
- ❑ The patient population that is addressable is 80%, based on a finding that two-thirds of the patients succumb to the disease within five years of diagnosis. We assume that patients with an advanced stage of the disease are not suitable candidates for Lpathomab therapy.
- ❑ Commercialization begins in 2017 with an initial penetration rate of 5% and rises over the next four years to a peak penetration of 20%. This reflects a good therapeutic index for Lpathomab and the availability of alternative treatments.
- ❑ The price of chronic therapy for IPF is comparable to that of effective antibodies against other life-threatening diseases, such as cancer.
- ❑ Lpath grants marketing rights to Lpathomab to a partner in 2011 in exchange for upfront and milestone payments of \$400 million and royalties at a 10% of its partner’s sales.

⁵⁵ Facts about idiopathic Pulmonary Fibrosis. Published by the Coalition for Pulmonary Fibrosis. (www.coalitionforpfp.org)

INCOME STATEMENT

<i>\$ in thousands, except per share data</i>	2009	2010	2011	2012	2013
<i>FY ending Dec. 31st</i>					
	2009	2010	2011	2012	2013
Total revenue	\$ 12,500	\$ 11,000	\$ 17,200	\$ 40,200	\$ 47,200
COGS	-	-	-	-	-
Gross profit	\$ 12,500	\$ 11,000	\$ 17,200	\$ 40,200	\$ 47,200
Operating expenses					
R&D	\$ 8,000	\$ 6,000	\$ 12,000	\$ 16,000	\$ 20,000
Selling & marketing	-	-	-	-	-
General & administrative	4,000	5,000	5,500	6,250	7,000
Total expense	12,000	11,000	17,500	22,250	27,000
Operating profit	\$ 500	\$ -	\$ (300)	\$ 17,950	\$ 20,200
Non-operating income/expense					
Interest expense	(10)	(10)	(10)	(10)	(10)
Interest income	50	50	100	200	200
Other	(3,000)				
Total non-operating	(2,960)	40	90	190	190
Pretax profit	\$ (2,460)	\$ 40	\$ (210)	\$ 18,140	\$ 20,390
Income tax				1,814	7,748
Net income	\$ (2,460)	\$ 40	\$ (210)	\$ 16,326	\$ 12,642
Earnings (loss) per share	\$ (0.03)	\$ 0.00	\$ (0.00)	\$ 0.20	\$ 0.15
Basic shares outstanding	54000	58000	65000	78000	80000
Diluted shares outstanding	75000	79000	82000	83000	84000

Assumptions:

- ❑ Lpath receives a \$28 million milestone payment in 1H 2010 when we believe Merck Serono will exercise its option for the ASONEP program following an extension of up to six-months from the original exercise date of October 2009. We assume the milestone payment is amortized equally over a five year period once received. Until the option exercise date, Lpath will receive payments of \$500,000 per month starting in November 2009 as part of the option extension agreement.
- ❑ Lpath received a \$3 million grant awarded by the Small Business Innovation Research (SBIR) Program sponsored by the National Cancer Institute (NCI) in June 2009. We believe Lpath will continue to seek similar non-dilutive funding opportunities.
- ❑ Lpath books royalties on its three drugs and incurs no marketing expense.
- ❑ Lpath spends \$8.0 million and \$6.0 million on R&D in 2009 and 2010, respectively, with the decline in 2010 due to Merck Serono assuming the development costs of ASONEP and an ocular partner assuming the costs of iSONEP. R&D begins to increase following 2010 as other pipeline candidates are advanced, and by 2013, R&D expense stabilizes at approximately 20% of revenue, in line with other drug companies' product development costs.
- ❑ General & administrative costs rise in 2010 and 2011, but increase at a somewhat slower rate thereafter. By 2013, G&A expenditures amount to 8%-9% of revenue.
- ❑ The company's effective tax rate is 10% in 2012, but thereafter the company books a tax liability for financial reporting purposes at 38%. (Note that the use of net operating loss carryforwards will minimize Lpath's cash obligations through 2013 according to our calculations.)
- ❑ Equity financings and grants of stock options increase the number of fully diluted shares outstanding.

HISTORICAL BALANCE SHEET

<i>\$ in thousands</i>	9/30/2009
ASSETS	
Current Assets	
Cash & equivalents	\$ 6,453
Accounts Receivable	551
Inventory	-
Other	147
Total Current Assets	<u>\$ 7,152</u>
Property & equipment	\$ 271
Intangible assets	833
Other	38
Total Assets	<u>\$ 8,293</u>
LIABILITIES	
Current Liabilities	
Accounts payable	\$ 488
Debt due	16
Other	1,400
Total Current Liabilities	<u>\$ 1,904</u>
Long-term debt	\$ 3
Other (1)	4,408
Total Long-Term Liabilities	<u>\$ 4,411</u>
Shareholders Equity	
Common Stock, par value	\$ 53
Additional Paid-In Capital	34,328
Accumulated Deficit	(32,402)
Treasury Stock	-
Total Shareholders Equity	<u>\$ 1,979</u>
Total liabilities & equity	<u>\$ 8,293</u>

Notes:

(1) Other long-term liabilities include \$4.4 million in warrants reclassified from equity starting January 1, 2009 pursuant to EITF 07-5. The warrant liability should not be subject to any future cash payments for settlement.

DISCOUNTED CASH FLOW (DCF) MODEL

Our DCF model, using a discount rate of 12.5%, suggests a value of \$5.16 for LPTN shares.

<i>\$ in thousands, except per share data</i>	2009	2010	2011	2012	2013
	2009	2010	2011	2012	2013
Revenue	\$ 12,500	\$ 11,000	\$ 17,200	\$ 40,200	\$ 47,200
Operating income	500	-	(300)	17,950	20,200
Net income	(2,460)	40	(210)	16,326	12,642
Depreciation/amortization	150	150	200	200	250
Stock-based compensation	200	200	200	400	1,200
Tax loss carryforwards	-	-	-	1,814	32,186
Capital expenditures	(140)	(150)	(200)	(200)	(225)
Other					
Total cash flow adjustments	210	200	200	2,214	33,411
Free cash flow	\$ (2,250)	\$ 240	\$ (10)	\$ 18,540	\$ 46,053
Risk-adjusted free cash flow	\$ (2,250)	\$ 240	\$ (10)	\$ 3,708	\$ 9,211

Discount Rate	Discounted Cash Flows (2008 - 2023)	PV of Terminal Value at a Perpetual growth rate of rFCF			Enterprise Value		
		2.0%	3.0%	4.0%	2.0%	3.0%	4.0%
7.5%	\$307,741.81	\$ 652,974	\$ 805,904	\$ 1,046,222	\$960,716	\$1,113,646	\$1,353,964
10.0%	\$234,230.47	\$ 317,984	\$ 366,973	\$ 432,292	\$552,215	\$601,204	\$666,523
12.5%	\$180,094.51	\$ 172,945	\$ 193,024	\$ 217,827	\$353,040	\$427,254	\$452,058
15.0%	\$139,810.26	\$ 100,456	\$ 109,894	\$ 121,048	\$240,266	\$344,124	\$260,859
17.5%	\$109,532.73	\$ 61,022	\$ 65,870	\$ 71,436	\$170,555	\$300,100	\$180,969

Discount Rate	Net Debt	Total Equity Value			Value per Diluted Share		
		2.0%	3.0%	4.0%	2.0%	3.0%	4.0%
7.5%	\$ (6,434)	\$967,150	\$1,113,646	\$1,360,398	\$ 11.51	\$ 13.26	\$ 16.20
10.0%	(6,434)	\$558,649	\$607,638	\$672,957	\$ 6.65	\$ 7.23	\$ 8.01
12.5%	(6,434)	\$359,474	\$433,689	\$458,492	\$ 4.28	\$ 5.16	\$ 5.46
15.0%	(6,434)	\$246,700	\$350,559	\$267,293	\$ 2.94	\$ 4.17	\$ 3.18
17.5%	(6,434)	\$176,989	\$306,535	\$187,403	\$ 2.11	\$ 3.65	\$ 2.23

Discount Rate	Terminal Value as % Enterprise Value			Implied EBITDA Multiple		
	2.0%	3.0%	4.0%	2.0%	3.0%	4.0%
7.5%	68.0%	72.4%	77.3%	11.53	14.23	18.47
10.0%	57.6%	61.0%	64.9%	7.93	9.15	10.77
12.5%	49.0%	45.2%	48.2%	6.04	6.74	7.61
15.0%	41.8%	31.9%	46.4%	4.88	5.34	5.88
17.5%	35.8%	21.9%	39.5%	4.09	4.42	4.79

DISCLOSURES

ANALYST(S) CERTIFICATION: The analyst(s) responsible for covering the securities in this report certify that the views expressed in this research report accurately reflect their personal views about Lpath, Inc. (the “Company”) and its securities. The analyst(s) responsible for covering the securities in this report certify that no part of their compensation was, is, or will be directly or indirectly related to the specific recommendation or view contained in this research report.

MEANINGS OF RATINGS: Our rating system is based upon 12 to 36 month price targets. **BUY** describes stocks that we expect to appreciate by more than 20%. **HOLD** describes stocks that we expect to change plus or minus 20%. **SELL** describes stocks that we expect to decline by more than 20%. **SC** describes stocks that Griffin Securities has **Suspended Coverage** of this Company and price target, if any, for this stock, because it does not currently have a sufficient basis for determining a rating or target and/or Griffin Securities is redirecting its research resources. The previous investment rating and price target, if any, are no longer in effect for this stock and should not be relied upon. **NR** describes stocks that are **Not Rated**, indicating that Griffin Securities does not cover or rate this Company.

DISTRIBUTION OF RATINGS: Currently Griffin Securities has assigned BUY ratings or NO RATINGS on all of the companies it covers. The Company has provided investment-banking services for 17% of companies in which it has had BUY ratings in the past 12 months, 0% for companies in which it has had NR or no coverage in the past 12 months or has suspended coverage (SC) in the past 12 months.

MARKET MAKING: Griffin Securities does not maintain a market in the shares of this Company or any other Company mentioned in the report.

COMPENSATION OR SECURITIES OWNERSHIP: The analyst(s) responsible for covering the securities in this report receive compensation based upon, among other factors, the overall profitability of Griffin Securities, including profits derived from investment banking revenue. The analyst(s) that prepared the research report did not receive any compensation from the Company or any other companies mentioned in this report in connection with the preparation of this report. The analysts responsible for covering the securities in this report currently do not own common stock in the Company, but in the future may from time to time engage in transactions with respect to the Company or other companies mentioned in the report. However, a member of an analyst’s household holds warrants to purchase shares of the Company common stock and an account in which a member of an analyst’s household has a financial interest holds warrants to purchase shares of the Company common stock. Griffin Securities from time to time in the future may request expenses to be paid for copying, printing, mailing and distribution of the report by the Company and other companies mentioned in this report. The Company is currently a client of Griffin Securities, Inc. Griffin Securities’ services for the Company consist of non-investment banking securities-related services and non-securities services. Griffin Securities has received compensation from the Company in the past 12 months for non-investment banking services. Griffin Securities expects to receive, or intends to seek, compensation for investment banking and non-investment banking services from the Company in the next three months.

PRICE CHART



8/31/2007 – Initiating Coverage: share price: \$1.75; rating: BUY; 12-month price target: \$6.00. **10/29/08** – Updating Coverage: share price: \$0.99; rating: BUY; 12-month price target: \$7.00. **11/20/09** – Updating Coverage: share price: \$0.80; rating: BUY; 12-month price target: \$5.00.

FORWARD-LOOKING STATEMENTS: This Report contains forward-looking statements, which involve risks and uncertainties. Actual results may differ significantly from such forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in the “Risk Factors” section in the SEC filings available in electronic format through SEC Edgar filings at www.SEC.gov on the Internet.

GENERAL: Griffin Securities, Inc. (“Griffin Securities”) a FINRA member firm with its principal office in New York, New York, USA is an investment banking firm providing corporate finance, merger and acquisitions, brokerage, and investment opportunities for institutional, corporate, and private clients. The analyst(s) are employed by Griffin Securities. Our research professionals provide important input into our investment banking and other business selection processes. Our salespeople, traders, and other professionals may provide oral or written market commentary or trading strategies to our clients that reflect opinions that are contrary to the opinions expressed herein, and our proprietary trading and investing businesses may make investment decisions that are inconsistent with the recommendations expressed herein.

Griffin Securities may from time to time perform corporate finance or other services for some companies described herein and may occasionally possess material, nonpublic information regarding such companies. This information is not used in preparation of the opinions and estimates herein. While the information contained in this report and the opinions contained herein are based on sources believed to be reliable, Griffin Securities has not independently verified the facts, assumptions and estimates contained in this report. Accordingly, no representation or warranty, express or implied, is made as to, and no reliance should be placed on, the fairness, accuracy, completeness or correctness of the information and opinions contained in this report.

The information contained herein is not a complete analysis of every material fact in respect to any company, industry or security. This material should not be construed as an offer to sell or the solicitation of an offer to buy any security in any jurisdiction where such an offer or solicitation would be illegal. We are not soliciting any action based on this material. It is for the general information of clients of Griffin Securities. It does not take into account the particular investment objectives, financial situations, or needs of individual clients. Before acting on any advice or recommendation in this material, clients should consider whether it is suitable for their particular circumstances and, if necessary, seek professional advice. Certain transactions - including those involving futures, options, and other derivatives as well as non-investment-grade securities - give rise to substantial risk and are not suitable for all investors. The material is based on information that we consider reliable, but we do not represent that it is accurate or complete, and it should not be relied on as such. The information contained in this report is subject to change without notice and Griffin Securities assumes no responsibility to update the report. In addition, regulatory, compliance, or other reasons may prevent us from providing updates.

DISCLOSURES FOR OTHER COMPANIES MENTIONED IN THIS REPORT: To obtain applicable current disclosures in electronic format for the subject companies in this report, please refer to SEC Edgar filings at www.SEC.gov. In particular, for a description of risks and uncertainties related to subject companies’ businesses in this report, see the “Risk Factors” section in the SEC filings.