Zacks Small-Cap Research

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# Spotlight Innovation (STLT-OTC)

## STLT: Crotoxin Trial Part 1 Data Upcoming, Part 2 to Commence Early 2016

| | |
|---|---|
| **Current Recommendation** | **Hold** |
| Prior Recommendation | N/A |
| Date of Last Change | 08/11/2015 |
| Current Price (08/24/15) | $1.05 |
| **Target Price** | **$1.70** |

## OUTLOOK

Spotlight is involved in identifying, acquiring/licensing and developing early-stage life sciences-related technologies and products. They recently acquired two separate companies which brought on promising early-stage clinical development of compounds that may have applications in the treatment of cancer, kidney disease and infectious diseases. One of the main focuses is on development of certain toxins found in snake venom for therapeutic applications in cancer and chronic kidney disease (CKD). These toxins have shown promise in early stage studies as cancer-fighting and pain relieving agents. STLT expects to initiate additional clinical trials in the near-term. The other major focus is with a platform technology called Immunoplex which is being developed to improve vaccine efficacy by using more efficient targeting and delivery. Immunoplex is in preclinical development for certain infectious diseases including influenza as well as for cancers of the breast, prostate and skin (melanoma).

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$2.00** |
| **52-Week Low** | **$1.05** |
| **One-Year Return (%)** | **-47.5** |
| **Beta** | **N/A** |
| **Average Daily Volume (sh)** | **14** |
| **Shares Outstanding (mil)** | **14** |
| **Market Capitalization ($mil)** | **$15** |
| **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 2015 Estimate** | **N/A** |
| **P/E using 2016 Estimate** | **N/A** |
| **Zacks Rank** | **N/A** |

| | |
|---|---|
| **Risk Level** | **N/A,** |
| **Type of Stock** | **Small-Growth** |
| **Industry** | **Med/Dental-Supp** |

## ZACKS ESTIMATES

**Revenue**
(in '000s of $)

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

**Earnings per Share**

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2013 | -$0.01 A | -$0.01 A | -$0.01 A | -$0.83 A | -$0.96 A |
| 2014 | -$0.01 A | -$0.13 A | -$0.07 A | -$0.07 A | -$0.28 A |
| 2015 | -$0.07 A | -$0.07 A | -$0.07 E | -$0.08 E | -$0.30 E |
| 2016 | | | | | -$0.28 E |

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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## WHAT'S NEW…

### Q2 10-Q Filed, Part 2 of Phase I Crotoxin Cancer Trial Expected to Start Early 2016

Spotlight filed their 10-Q for the second quarter ending June 30th. There were no surprises to the financials or otherwise. Operating expenses were $737k, inline with our $722k estimate. Net loss and EPS were $1.0 million and ($0.07), slightly better than our $1.2 million and ($0.08) estimates, with the difference almost entirely attributable to interest expense coming in lower than what we had modeled.

This morning (8/24) Spotlight provided an update to their expected timelines for the Phase I trial assessing Crotoxin in the treatment of cancer. The company notes that data from Part 1 of the study is now being aggregated and prepared for analysis with results potentially available in November. Spotlight is now making preparations to commence Part 2 of the study, which they think could commence in January 2016.

Below is a refresher on the trial which we first detailed in our August 12th initiation report on Spotlight…

**Celtic Biotech's Phase I open label crotoxin study**

Celtic initiated a Phase I open label clinical trial in 2011. The protocol, per clinicaltrials.gov, called for crotoxin to be administered intravenously to (up to) 24 stage IV cancer patients. The study, titled *Crotoxin in Patients with Advanced Cancer Using an Intravenous Route of Administration*, hopes to address some of the questions that came out of an earlier study (Cura et al., which we discuss in detail in our initiation report) - including whether adverse side effects could be tempered through induction of tolerance and, concurrently, whether the cancer would show effective response to higher crotoxin doses. Unlike the earlier study, Celtic's Phase I study has used intra-patient dose escalation. In addition, the previous study used intramuscular injection while this study administered crotoxin via intravenous (IV) drip which is intended to reduce toxic side effects. This study also used a maximum dose which was much higher than the previous study's MTD (0.32mg/$m^2$ vs. 0.21mg/$m^2$).

Primary objective is to "assess whether human subjects can be made tolerant to intravenously administered Crotoxin and achieve higher and more therapeutically effective dose levels without the previously reported adverse effects associated with bolus i.m. (intramuscular) administration." Secondary objective is evidence of anti-cancer response to crotoxin.

The trial was separated into two cohorts. While both cohorts, per the initial protocol, were to enroll up to 12 patients each, Part 1 enrolled 6 patients and Part 2, which is expected to commence in January 2016, is still expected to enroll up to 12 patients. Below is from the original trial protocol. However, Spotlight / Celtic has yet to announce the final part 2 protocol, which may be amended from the original - we expect this will be announced prior to initiation of part 2.

- cohort 1: receive crotoxin doses of 0.04mg/$m^2$ to 0.32mg/$m^2$ via two hours of I.V. drip for five consecutive days followed by two off. Doses be escalated to a maximum of 8 levels over the course of 40 treatment days (five days per dose level). MTD defined as the dose level where no toxicity is observed for three consecutive patients or not more than one DLT is observed for six patients.
- cohort 2: receive the same dose levels as cohort 1 but dose escalation will be more rapid. The eight doses will be escalated over 27 days (instead of 40). This, however, may be amended - see below.

Part 1 of the study was completed but Part 2 was subsequently suspended for reasons, per the notation on clinicaltrials.gov, related to "funding issues." However, per the company's August 24th press release, data from Part 1 of the study is now being aggregated and prepared for analysis with results potentially available in November. Spotlight is now making preparations to commence Part 2 of the study, which they think could commence early next year - the company recently engaged ImmunoClin, Inc., a contract research organization, to manage it.

Per Spotlight's July 21 press release announcing consummation of a Clinical Study Management Agreement with Immunoclin to manage the second part of the study, protocol of the second part may be amended from the original - details of which we think should be forthcoming. The press release did provide some detail on the second part including; expected enrollment of 12 patients at 3 sites in France, treatment duration is expected to be 37 days with 30-day follow-up and total duration of the study expected to be ~18 months.

## SNAPSHOT

Spotlight Innovation, Inc. (STLT), headquartered in Des Moines, Iowa specializes in identifying, acquiring/licensing and developing early-stage life sciences-related technologies and products. Their specific strategy involves cultivating relationships with leading research universities and institutions, acquiring and further developing high-potential intellectual property and then monetizing this through partnerships. Spotlight, which went public and began trading on the OTC exchange in early 2014, recently acquired two separate companies which brought on promising early-stage clinical development of compounds that may have applications in the treatment of cancer, kidney disease and infectious diseases.

STLT acquired Celtic Biotech (Celtic), a small research-oriented life sciences company, in June 2014. Celtic's main focus has been the development of certain compounds found in snake venom for therapeutic applications in cancer and chronic kidney disease (CKD). In early-stage clinical trials, crotoxin, a toxin derived from the South American rattlesnake, has shown efficacy in the reduction of both pain and tumor mass in patients with cancer. Celtic's other development effort has been with cardiotoxin, found in the venom of Chinese cobras, for applications in cancer and CKD.

In June 2015 Spotlight acquired controlling interest in Memcine Pharmaceuticals, a biotech company located in the University of Iowa Research Park. Memcine has a platform technology called Immunoplex which is being developed to improve vaccine efficacy by using more efficient targeting and delivery. Immunoplex is in preclinical development for certain infectious diseases including influenza as well as for cancers of the breast, prostate and skin (melanoma).

Celtic is looking to further beef up their snake venom-based pipeline and recently consummated a deal to acquire rights to crotamine from Instituto Butantan. Butantan is the largest biopharmaceutical organization in Brazil which has done extensive research on crotamine, a cell-penetrating peptide derived from rattlesnake venom. In July 2015 STLT announced an agreement between Celtic Biotech and Emory University whereby Emory will design and conduct a phase I study for use of crotamine as a radiopharmaceutical imaging agent for lung cancer.

Other recent developments include the engagement of ImmunoClin, a contract research organization (CRO), to manage the second of two parts of a phase I clinical study assessing crotoxin for the treatment of cancer. Results of part one are now being aggregated and prepared for analysis with results potentially available in November. The second part is expected to commence early next year.

In June Celtic retained the FreeMind Group to seek public and private grant and contract funding opportunities to help fund development of the pipeline, including this phase I crotoxin study. Freemind bills itself as "the premier international consulting firm specializing in assisting life science organizations secure non-dilutive funding from U.S. federal agencies and private foundations."

## Current Pipeline

| Drug Candidate | Mechanism of Action | Indication | Preclinical | Phase I | Phase II | Phase III | Market |
|---|---|---|---|---|---|---|---|
| **CELTIC BIOTECH** | | | | | | | |
| Crotoxin | Triggers apoptosis | Lung cancer, Melanoma, Renal cancer, Breast cancer | | | Q2 2017 | Q2 2018 | Q3 2019 |
| VRCTC | Multiple | Leukemia, Lymphoma, Squamous cell cancer, Pancreatic cancer | | | Q4 2017 | Q4 2018 | Q2 2020 |
| Crotalin | Triggers apoptosis | Colon cancer, Pancreatic cancer, Brain cancer | Q1 2017 | Q2 2018 | Q2 2019 | Q1 2020 | Q2 2021 |
| Crotalin | Triggers apoptosis | Canine tumors | Q1 2016 | n/a | n/a | n/a | Q1 2018 |
| Cardiotoxin | Anti-inflammatory | Chronic kidney disease | | | Q1 2016 | Q1 2017 | Q4 2018 |
| Cardiotoxin | Adjuvant | Vaccines | | Q4 2016 | | | |
| Cardiotoxin | PK inhibitor | with chemo | | Q4 2017 | | | |
| Crotamine | Multiple | Cancer imaging | | Q2 2017 | Q2 2018 | | |
| Crotamine | Cell Pene. Peptide | Gene therapy | Q2 2017 | Q2 2018 | | | |
| **MEMCINE PHARMACEUTICALS** | | | | | | | |
| Danuplex | | Breast cancer | | | | | |
| FluInt (Vaccine) | | Influenza | | | | | |

*Dates indicate tentative start dates*

KEY
Completed
In Process

SPOTLIGHT INNOVATION

SOURCE: Spotlight Innovation

## BACKGROUND

**Snake Venom**
Snake venom contains certain proteins, peptides, enzymes and toxins. Not all snake venom is the same or even necessarily similar. Some venoms elicit no ill effects to humans while others are highly toxic and deadly. Geographic characteristics such topography, climate and the kinds of other local indigenous wildlife influence the types of snakes that inhabit particular areas of the world. This has also influenced, through evolution, the type of venom produced by snakes around the globe.

Toxic snake venom can cause a variety of adverse effects and functions to paralyze or otherwise immobilize prey and then to aid in digestion. Venom is divided into three specific categories based on the effect they have;

- **Neurotoxic**: affects the nervous system. Mostly found in elapids (coral, cobras and many Australian snakes)
- **Hemotoxic**: affects the cardiovascular system. Mostly found in vipers, with some exceptions
- **Cytotoxic**: affects the cells and tissue at the site of the bite

There are several kinds of toxins in snake venom but the two major classes are neurotoxins and hemotoxins. Neurotoxins are mostly found in elapids such as coral snakes, cobras and most Australian snakes, although there are some exceptions. Hemotoxins are mostly found in vipers such as rattlesnakes copperheads and cottonmouths but, again, there are some exceptions. Certain enzymes (proteins) in the venom serve specific functions and may include attacking the nervous system to paralyze the prey, breakdown of cell structures and inhibition of blood clotting, among others.

**Snake Venom As Cancer Therapeutic**
But the toxicity of snake venom appears to have therapeutic qualities as well, including attacking and killing tumor cells. In fact, the idea of using animal venom to fight cancer is not new. HuChanSu, a traditional Chinese medicine which utilizes toad venom to target cancer cells, has been used for over 1,000 years. And alternative medicine practitioners in Cuba have used venom from scorpions to treat brain cancer. More recently there has been much more extensive research dedicated to how animal venom, and particularly snake venom, may be an effective agent to fight cancer.

Cancer growth and metastasis occurs due to rapid cell division and angiogenesis which is unimpeded due to lack of sufficient apoptosis (i.e. programmed cell death) of the cancer cells. The purpose of many current anti-cancer therapies, including chemotherapy, is to target and kill cancer cells. However, chemotherapy does not discriminate between healthy and malignant cells which results in chemotherapy-related sickness. And another major drawback of chemotherapy is that it is largely ineffective if the cancer has metastasized.

Research over the last few decades has discovered that snake venom has anticancer efficacy as well as pain relieving qualities. While the specific mode of action relative venom's cancer fighting effect is still not fully understood, studies have shown that certain proteins and enzymes isolated from snake venom not only induce cell apoptosis and hinder rapid cell division, but also specifically targets cancer cells with a more benign effect on healthy cells and tissue.

Many of the leading venom therapy researchers are of Indian/Asian descent which likely reflects the relative concentration of venomous snakes in that area of the world. A paper titled, *Therapeutic Potential of Snake Venom in Cancer Therapy: Current Perspectives*, published in February 2013 in the Asian Pacific Journal of Tropical Biomedicine by researchers at the Institute of Pharmacy, at Nirma University in India summarized findings of recent research of snake venom as a cancer therapy. The focus of most of the research to-date has been on snake venom's ability to promote cell apoptosis and proliferation. A wide variety of snake venoms have shown anti-cancer efficacy on several tumor types including cancers of the breast, lung, colon, brain, blood, cervix, stomach, skin and others. The following are some of the findings from the 50+ studies cited by the authors of the paper;

- ACTX-6, a protein from the venom of Agkistrodon snakes (North American pit vipers such as cottonmouth, copperheads and cantils), showed cytotoxic effects (i.e. - toxicity to living cells) to various cancer cells in-vitro. The study found that ACTX-6 promoted cell death by stimulation of certain proteins (Fas / FasL) that are responsible for inducing apoptosis

- ACTX-8, also an Agkistrodon snake protein, showed cytotoxicity on cervical cancer cells and inhibited cell proliferation in-vitro. The study suggested that the mitochondrial pathway was an important factor in ACTX-8 induced apoptosis
- An L-amino acid oxidase from venom of Bothrops leucurus (Brazilian pit vipers) inhibited blood coagulation and demonstrated cytotoxicity of stomach cancer, adeno carcinoma and colorectal cancer cell lines. The method of action resulting in cell death was attributed to the generation of high amounts of the enzyme $H_2O_2$
- Venom of Ophiophagus hanna (king cobra) was purified. L-amino acid oxidase was also shown to have cytotoxic properties. It demonstrated toxicity to stomach cancer, murine (rodent) melanoma, fibrosarcoma, colorectal cancer and hamster ovary cells. Cytoxicity reduced the level of cell proliferation by 74%. Method of action is thought to be attributed to inhibition of thymidine incorporation
- Venom of Naja kaouthia (monocled cobra) was purified. Studies on human leukemia cells showed that it significantly inhibited cell proliferation and induced apoptosis. In addition the purified venom showed low toxicity on normal human leukocytes
- A cytotoxic and antioxidant protein (NN32) in Naja naja (spectacled cobra) venom demonstrated cytotoxicty to Ehrlich ascites carcinoma (or EAC, a cancer specific to rodents). When injected in EAC mice it increased survival and reduced tumor volume and weight
- BJcuL, a lectin isolated from venom of Bothrops jararacussu (South American pit viper) was shown to (weakly) adhere to and suppress the viability of cells from human metastatic breast cancer and ovarian cancer
- A separate study showed BJcuL induced apoptosis in human gastric carcinoma through inhibition of cell adhesion
- Apoxin protein-1 (OHAP-1) was extracted from the venom of Trimeresurus flavoviridis (Japanese tree viper) and tested on brain cancer cells of rats and humans. OHAP-1 inhibited cell growth of all cell lines and showed inducement of apoptosis
- Venom from Lapemis curtus (Shaw's sea snake) was able to inhibit cancer cell proliferation in EAC albino mice and HeLa and Hep2 tumor cell cultures. The venom significantly reduced tumor growth in the mice and increased their length of survival by over 200%
- Disintegrins are small proteins found in viper venom that inhibit blood coagulation and cell-to-cell adhesion. Breast and prostate cancer often spread to bone. Researchers found that disintegrins strongly inhibited the adhesion, migration and invasion of tumor cells in mice as well as inhibited growth of human breast cancer cells in bone
- Cardiotoxin III, a peptide isolated from Naja naja atra (Chinese cobra) induced cell apoptosis in human breast cancer cell lines

## CROTOXIN

Celtic's main focus has been the development of two specific snake venom toxins; crotoxin, as a pain and cancer therapeutic, and cardiotoxin, for cancer and chronic kidney disease.

**Crotoxin**, a cytotoxic phospholipase isolated from the venom of Crotalus durissus terrificus (South American rattlesnake), has shown efficacy in the reduction of both pain and tumor mass in clinical trials with cancer patients. Crotoxin is comprised of two subunits, A (crotapotin) and B (crotactine). Subunit B is toxic while subunit A is not. Studies have indicated that crotapotin has a specific binding affinity for cancer cells while crotactine induces apoptosis by causing collapse of the mitochondrial membrane and release of certain proteins essential to the programmed cell death process.

**South American Rattlesnake**



SOURCE: scielo.br

Crotoxin has been evaluated as a therapeutic in several animal and human studies which have been published in peer-reviewed journals. Cancer-killing and pain reduction efficacy is clearly demonstrated in the pre-clinical and clinical studies alike which we think may bode well for positive results in larger human studies. And while neurotoxic side effects are inherent with snake venom, these appear to be temporary and reversible with discontinuation of treatment. We summarize some of these animal and human studies and their findings below;

**Animal / In-vitro studies:**

***Contributions of autophagic and apoptotic mechanisms to CrTX-induced death of K562 cells***[1]

In-vitro study of crotoxin in chronic myeloid leukemia cell line, K5652, cells. Crotoxin inhibited viability of K562 cells by collapse of the mitochondrial membrane potential, release of cytochrome c (an intermediate in apoptosis) and activation of caspase-3 (which plays an important role in apoptosis)

**Opiate and acetylcholine-independent analgesic actions of crotoxin isolated from crotalus durissus terrificus venom**[2]

The analgesic effects of crotoxin were evaluated following injection into mice and rats. Pain was evaluated with (scientifically accepted) hotplate, acetic acid writhing and tail-flick tests. The study found crotoxin produced significant analgesic effects which was mediated by the central nervous system. In addition, atropine (muscle relaxant, antispamodic) and naloxene (opiate pain killer) did not block these analgesic effects

**Autophagy is involved in cytotoxic effects of crotoxin in human breast cancer cell line MCF-7 cells**[3]

Human breast cancer cells which are deficient of caspase-3 (MCF-7 cells) were treated with crotoxin. Results showed crotoxin activated autophagy (i.e. cell degradation) and increased apoptosis, inhibiting the viability of the breast cancer cells

[1] Yan CH, Liang ZQ, Gu ZL, Yang YP, Reid P, Qin ZH. *Contributions of autophagic and apoptotic mechanisms to CrTX-induced death of K562 cells*. Toxicon. 2006 Apr;47(5):521-30. Epub 2006 Mar 15

[2] Zhang HL, Han R, Chen ZX, Chen BW, Gu ZL, Reid PF, Raymond LN, Qin ZH. Opiate and acetylcholine-independent analgesic actions of crotoxin isolated from crotalus durissus terrificus venom. Toxicon. 2006 Aug;48(2):175-82. Epub 2006 Apr 28

[3] Yan CH, Yang YP, Qin ZH, Gu ZL, Reid P, Liang ZQ. Autophagy is involved in cytotoxic effects of crotoxin in human breast cancer cell line MCF-7 cells. Acta Pharmacol Sin. 2007 Apr;28(4):540-8

**Crotoxin enhances the antitumor activity of gefinitib (Iressa) in SK-MES-1 human lung squamous carcinoma cells[4]**

Human lung squamous cancer cells which had become resistant to EGFR tyrosine kinase inhibitors (common cancer drugs) were treated with crotoxin. Results showed crotoxin caused apoptosis of the cancer cells and in addition, when combined with Iressa (an EGFR-TK inhibitor), the combination enhanced the antitumor effects of Iressa

**Growth inhibitory effects and molecular mechanisms of crotoxin treatment in esophageal Eca-109 cells and transplanted tumors in nude mice[5]**

Human esophageal carcinoma cells were treated with crotoxin in-vitro and with the cancer cells transplanted in mice. Results showed crotoxin inhibited cancer cell growth in vitro by inducing apoptosis and G1 block. In the mice experiment crotoxin resulted in inhibition of cancer cell growth

**Human studies:**

**Phase I and Pharmacokinetics Study of Crotoxin (Cytotoxic PLA2, NSC-624244) in Patients with Advanced Cancer**

Published in April 2002 in the peer-reviewed journal Clinical Cancer Research in April 2002. The study enrolled 26 patients (23 of which were ultimately evaluable) with solid tumors resistant to conventional cancer therapies. Enrollment consisted of cancers of the breast (n=4), gastrointestinal (n=7), non-small cell lung (n=3), squamous cervical (n=2), prostate (n=2) and one patient had several types of cancer including thyroid, larynx, bladder and head/neck cancer.

Primary objectives of the study were to identify the dose-limiting toxicity (DLT), the maximum tolerated dose (MTD) and to establish the pharmacokinetic profile for crotoxin. DLT was defined as meeting predetermined levels of toxicity-induced; loss of coordination, nystagmus (rapid, involuntary eye movements), anxiety, as well as any other toxicity of grade 3 or higher on the National Cancer Institute Common Toxicity Criteria (on a scale of 1 to 5; 1=mild, 2=moderate, 3=severe, 4=life-threatening, 5=death).

Crotoxin was injected intramuscularly daily for 30 days at doses ranging from 0.03mg/$m^2$ to 0.22mg/$m^2$ . One patient was evaluated at the lowest dose to ensure no toxicity - which there was none after 3 weeks. Planned escalations were at 0.06mg/$m^2$, 0.12mg/$m^2$ and 0.18mg/$m^2$ . Three patients were enrolled at each dose level (intrapatient dose escalation was not permitted). Additional dose increases were to 0.21mg/$m^2$ and 0.22mg/$m^2$.

If two or more patients at a given dose level met the criteria for DLT, that dose level was identified as the DLT. MTD was defined as one level below the DLT level. When the MTD was identified, additional patients were enrolled to further evaluate the MTD level. Summary of the results follow;

Neurological Toxicity (also see table below);

- no significant toxicity found up to 0.12mg/$m^2$ dose level
- grade 2 diplopia became prevalent at dose levels 0.18mg/$m^2$ and 0.21mg/$m^2$ . This lasted for 4-12 hours
- almost all patients had diplopia which appeared intermittently but was completely gone by day 21
- study authors consider the diplopia as "nonlimiting" as it vanished as least 12 hours before the next dose, progressively lasted for shorter durations and was completely gone by day 21
- diplopia was caused by partial (and temporary) paralysis of the external eye muscles
- diplopia at dose level of 0.22mg/$m^2$ was sometimes accompanied with other eye conditions including abnormal alignment (strabismus) and drooping eyelids (ptosis), indicating higher doses increase neuromuscular impairment

[4] Wang JH, Xie Y, Wu JC, Han R, Reid PF, Qin ZH, He JK. Crotoxin enhances the antitumor activity of gefinitib (Iressa) in SK-MES-1 human lung squamous carcinoma cells. Oncol Rep. 2012 May;27(5):1341-7. doi: 10.3892/or.2012.1677. Epub 2012 Feb 6

[5] He JK, Wu XS, Wang Y, Han R, Qin ZH, Xie Y. Growth inhibitory effects and molecular mechanisms of crotoxin treatment in esophageal Eca-109 cells and transplanted tumors in nude mice. Acta Pharmacol Sin. 2013 Feb;34(2):295-300. doi: 10.1038/aps.2012.156. Epub 2012 Dec 3

- at 0.22mg/m$^2$ dose level there were signs of grade 2 incoordination and nystagmus as well as anxiety. These were considered signs of severe crotoxin toxicity so 0.22mg/m$^2$ was deemed the DLT
- MTD was set at 0.21mg/m$^2$ . The authors recommended a dose of 0.18mg/m$^2$ for follow-on phase II studies
- even at the MTD level any neurotoxic-related temporary paralysis was limited to the eyes (i.e. - did not affect respiratory muscles) and this was fully reversible
- tolerance to the toxicity was observed with almost all of the patients receiving the 0.21mg/m$^2$ dose having anti-crotoxin antibodies present in their blood after the fourth week of treatment. Antibody production was expected as an immune response to administration of a heterologous protein. While tolerance will reduce unwanted side effects, it will also likely reduce cancer-fighting efficacy

*Table 2* Neurotoxicity in patients treated with crotoxin

| Dose (mg/m$^2$) | Days of treatment | Neurotoxicity[a] grade (study days) | | | |
|---|---|---|---|---|---|
| | | Diplopia[b] | Palpebral ptosis | Nystagmus | Anxiety |
| 0.18 | 30 | 2 (9–19) | — | — | — |
| 0.18 | 30 | 2 (6–14) | | | |
| 0.18 | 30 | 2 (2–10) | | | |
| 0.21 | 30 | 2 (2–20) | | | |
| 0.21 | 30 | 2 (1–14) | | | |
| 0.21 | 90 | 2 (11–21) | | | |
| 0.22 | 30 | 2 (2–4) | (19–22) | 2 (15–16) | 2 (15), 3 (16) |
| 0.22 | 90 | 2 (6–14) | — | 2 (16–17) | 3 (17) |
| 0.22 | 30 | 2 (8) | — | — | — |
| 0.22 | 30 | 2 (4, 5) | | | |
| 0.22 | 30 | 2 (2–21) | (18–20) | 2 (15) | 3 (15) |
| 0.22 | 30 | 2 (8–21) | (12–18) | 2 (19–20) | 2 (19); 3 (20) |
| 0.21 | 2 | | Died on study day 3[c] | | |
| 0.21 | 90 | 2 (2–21) | | | |
| 0.21 | 60 | 2 (2–11) | | | |
| 0.21 | 90 | 2 (1–5) | | | |
| 0.21 | 30 | 2 (10–21) | Discharged on study day 31[d] | | |
| 0.21 | 8 | 2 (4–5) | Abandoned protocol on day 8[e] | | |

[a] No neural toxicity was observed at doses up to 0.18 mg/m$^2$.
[b] Diplopia appeared intermittently within the study days indicated in parenthesis.
[c] This patient died on study day 3 of pulmonary edema.
[d] Patient had a mild allergic reaction on study day 3 and a grade 3 anaphylactic reaction on day 31.
[e] Patient abandoned the protocol on study day 8, unable to adapt to the obligatory in-patient condition required by this study.

SOURCE: footnote[6]

Non-Neurological Toxicity:

Patients also exhibited non-neurological side effects which were similar to what has been observed in animal studies. These included sialorrhea (excess saliva), urination, diarrhea, an increase in plasma levels. Similar to the neurotoxic side effects, these non-neurological symptoms disappeared with discontinuation of treatment

Pain and Disease Response:

- Pain: 18 of the 23 evaluable patients reported a progressive and significant decrease or complete disappearance of cancer-related pain beginning with the second or third week of treatment. Pain decrease was measured by the reduction of analgesics used and from input from the patients. Individual highlights of the pain response included a) Ewing's sarcoma patient showed increased mobility and increased muscular strength and b) patient with rectal cancer and pelvic invasion stopped his scheduled morphine after three weeks on one of the lower doses (0.12mg/m$^2$) of crotoxin

[6] Cura JE, et al. *Phase I and Pharmacokinetics Study of Crotoxin(Cytotoxic PLA2, NSC-624244) in Patients with Advanced Cancer*. Clinical Cancer Research. Vol 8, 1033-1041, April 2002

- Disease Response: four patients showed no progression of their cancers and some of these it appeared that the cancer may have even reduced. An additional three patients showed a partial response. These include;
  - patient with colon cancer and hepatic (liver) metastases treated with 0.06mg/$m^2$ (i.e low dose) showed 40% reduction of the hepatic metastases over 60 days. The authors noted that the disease began to progress afterwards (although provided no other specifics)
  - fibrosarcoma patient with edema in both legs treated with 0.21mg/$m^2$ crotoxin for 117 days had edemas disappear
  - patient with cancer of the larynx, lymph node invasion and tumors on both sides of the neck showed reduced lymph node mass with 30-day treatment at 0.12mg/$m^2$ dose
  - patient with rectal cancer and pelvic invasion had unresectable (i.e. unable to be removed) tumor. After receiving 0.12mg/$m^2$ dose the tumor showed reduction in size at day 78 and was able to be removed
  - breast cancer patient with metastasis to the lungs and bones received 0.21mg/$m^2$ dose and on day 90 showed complete response in both lung and bone lesions which lasted for 6 months after treatment ended

Pharmacokinetic:

- Crotoxin was rapidly absorbed in the plasma after injection and distribution throughout the body was complete within about two hours
- Crotoxin was also rapidly eliminated from the body with ~95% of it eliminated within 24 hours. This rapid elimination is beneficial as it reduces the potential for cumulative toxicity (from subsequent injections)

**Celtic Biotech's Phase I open label crotoxin study**

Celtic initiated a phase I open label clinical trial in 2011. The protocol, per clinicaltrials.gov, called for crotoxin to be administered intravenously to (up to) 24 stage IV cancer patients. The study, titled *Crotoxin in Patients with Advanced Cancer Using an Intravenous Route of Administration*, hopes to address some of the questions that came out of the earlier study - including whether adverse side effects could be tempered through induction of tolerance and, concurrently, whether the cancer would show effective response to higher crotoxin doses. Unlike the trial discussed earlier, this study used intra-patient dose escalation. In addition, the previous study used intramuscular injection while this study administered crotoxin via intravenous (IV) drip which is intended to reduce toxic side effects. This study also used a maximum dose which was much higher than the previous study's MTD (0.32mg/$m^2$ vs. 0.21mg/$m^2$).

Primary objective is to "assess whether human subjects can be made tolerant to intravenously administered Crotoxin and achieve higher and more therapeutically effective dose levels without the previously reported adverse effects associated with bolus i.m. (intramuscular) administration." Secondary objective is evidence of anti-cancer response to crotoxin.

The trial was separated into two cohorts. While both cohorts, per the initial protocol, were to enroll up to 12 patients each, Part 1 enrolled 6 patients and Part 2, which is expected to commence in January 2016, is still expected to enroll up to 12 patients. Below is from the original trial protocol. However, Spotlight / Celtic has yet to announce the final part 2 protocol, which may be amended from the original - we expect this will be announced prior to initiation of part 2.

- cohort 1: receive crotoxin doses of 0.04mg/$m^2$ to 0.32mg/$m^2$ via two hours of I.V. drip for five consecutive days followed by two off. Doses be escalated to a maximum of 8 levels over the course of 40 treatment days (five days per dose level). MTD defined as the dose level where no toxicity is observed for three consecutive patients or not more than one DLT is observed for six patients.
- cohort 2: receive the same dose levels as cohort 1 but dose escalation will be more rapid. The eight doses will be escalated over 27 days (instead of 40). This, however, may be amended - see below.

Part 1 of the study was completed but Part 2 was subsequently suspended for reasons, per the notation on clinicaltrials.gov, related to "funding issues." However, per the company's August 24th press release, data from Part 1 of the study is now being aggregated and prepared for analysis with results potentially available in November. Spotlight is now making preparations to commence Part 2 of the study, which they think could commence early next year - the company recently engaged ImmunoClin, Inc., a contract research organization, to manage it.

Per Spotlight's July 21 press release announcing consummation of a Clinical Study Management Agreement with Immunoclin to manage the second part of the study, protocol of the second part may be amended from the original - details of which we think should be forthcoming. The press release did provide some detail on the second part including; expected enrollment of 12 patients at 3 sites in France, treatment duration is expected to be 37 days with 30-day follow-up and total duration of the study expected to be ~18 months.

**Spotlight's Patent-Protected Crotoxin Cancer Therapy Application:**

In January 2015 Celtic Biotech was granted U.S. patent #8,921,305, a method and use patent titled, *Crotoxin Administration for Cancer Treatment and Pain Relief*. Claims of the patent are reflective of the protocol of their phase I study. The bulk of the IP of this patent relates to the intra-patient dose escalation procedure used to deliver crotoxin. Specifically, claims of the patent are;

- method for **treating cancer** using crotoxin administered intravenously (injection or I.V. drip) with intra-patient dose escalation from 0.04mg/$m^2$ and up to a maximum of 0.32mg/$m^2$ . Each dose level is used for 3 - 5 days with step-up doses scheduled as 0.04, 0.12, 0.16, 0.20, 0.24, 0.28 and 0.32mg/$m^2$ Each successive dose escalation is predicated on there being no DLT from the prior dose and (in some cases ) is preceded by a two-day non-treatment period
- method for **treating pain** associated with cancer using crotoxin with the same protocol as that used for treating cancer. The pain can be associated with cancer, arthritis, multiple sclerosis or any variety of pain.

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## CARDIOTOXIN / VRCTC-310

Cardiotoxins, as the name suggest, are compounds that target and are toxic to the heart and its muscles, preventing the heart muscles from contracting. Cardiotoxin is found in the venom of the Naja naja atra cobra. Cardiotoxin III is what has been used in most animal and clinical studies for the treatment of cancer. It is a polypeptide consisting of 60 amino acids.

Several studies have indicated that Cardiotoxin induces apoptosis, although the mechanism by which cell death occurs includes a number of hypotheses. These include (some of which we have summarized in the animal studies discussion); activation of caspase-12 and c-Jun N-terminal kinase (JNK) pathway, influx of Ca2+ (i.e. calcium ions) influx, G1 stage proliferation, activation of endoplasmic-reticulum-associated protein degradation (ERAD), loss of mitochondrial viability, down regulation of NF-kB (i.e. certain proteins responsible for cell survival) and inactivation of the apoptosis pathways EGFR, P13K/AKT and JAK/STAT3.

VRCTC-310 is a combination of Crotoxin and Cardiotoxin. Preclinical studies[7,8,9] of VRCTC-310 have indicated affinity for high cytotoxic disease specificity and low neurotoxic side effects, particularly as compared to crotoxin. The compound has also been assessed in early-stage clinical studies for the treatment of cancer.

In a phase 1[10] study two patients suffering from advanced cancer were treated with VRCTC-310 at a weekly dose of 0.14mg/kg over a six week period. One patient, suffering from squamous cell skin cancer and who had "severely compromised" skin had a complete disappearance of the relapsed cancer following the VRCTC-310 treatment (which was applied at the site of the cancer). Patient 2 with local-advanced breast cancer experienced an over 80% reduction of the tumor following VRCTC-310 treatment. In addition, at a 133-day post-treatment follow-up, a complete response to the tumor mass was observed as was disappearance of the tumor mass and

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[7] Detolla L. et al. *Toxicity of the novel animal-derived anticancer agent, VRCTC-310: acute and subchronic studies in beagle dogs.* Toxicology. Vol 99. May 1995, 31-46

[8] Newman R. et al. *VRCTC-310 - A novel compound of purified animal toxins separates antitumor efficacy from neurotoxicity*. Investigational New Drugs. 11: 151-159, 1993

[9] Stanchi, NO et al. *One-month safety study of intraperitoneal VRCTC-310-Onco (crotoxin+cardiotoxin) in rats.* Arzneimittelforschung. 2000 Sep; 50(9):862-6

[10] Costa LA, Miles F, Araujo CE, Gonzalez S, and Villaruba VG*: Tumor regression of advanced carcinoma following intra-and/or peri-tumoral inoculation with VRCTC310 in humans: preliminary report of two cases.* Immunopharmacol. Immunotoxicol. 20 (1), 15-25 (Feb 1998)

reduction of inflammation of the lymphatic channels. The study was published in February 1998 in the journal Immunopharmacology and Immunotoxicology.

In another study, this one to determine the MTD, fifteen patients with refractory malignancies received escalating doses of VRCTC-310 which was administered via intramuscular injection daily for 30 consecutive days. Doses were escalated from 0.0025mg/kg to 0.023mg/kg. Two patients developed anaphylactoid reactions at the 0.023mg/kg dose and the MTD for that particular dosing protocol was determined to be 0.017mg/kg. This was also the recommended dose for phase 2 studies.[11] The study was published in October 1997 in the journal Anticancer Drugs.

**Cardiotoxin as CKD Therapy**

In March 2015 Celtic Biotech announced that they in-licensed worldwide (ex-China) rights to develop and market Cardiotoxin for the treatment of CKD. The patent-pending invention, licensed from Zheng-Hong Qin of Soochow University, China, is titled "Use of Cardiotoxin for the Treatment of Chronic Kidney Disease." Per terms of the licensing agreement, Celtic will pay a 7% royalty on any eventual sales of a product developed with the licensed technology.

Zheng-Hong was a lead investigator of an animal study investigating Cardiotoxin as a CKD therapeutic. The study, titled *Ameliorating Adriamycin-Induced Chronic Kidney Disease in Rats by Orally Administered Cardiotoxin from Naja naja atra Venom,* was published in April 2014 in the journal Evidence-Based Complementary and Alternative Medicine.

Following injection with adriamycin to induce CKD the rats received cardiotoxin doses of 45, 90 and 180 µg/kg body weight. Urine was collected once per week. After six weeks CKD-associated serum profiles were measured which included albumin, total cholesterol, phosphorus, blood urea nitrogen, and serum creatinine. Organ histology was also performed. The study demonstrated that rats which were induced with CKD showed improved levels of biological markers associated with kidney disease and reduced adriamycin-induced kidney pathology following administration of cardiotoxin. The authors concluded that, "These findings suggest that cardiotoxin is an active ingredient of Naja naja atra venom (NNAV) in protecting adriamycin nephropathy. Cardiotoxin itself or in combination with other active components of NNAV may be used for treatment of chronic kidney disease."

> **CKD Market:** The Centers for Disease Control and Prevention estimate that more than 10% of American adults, or greater than 20 million people, suffer from various levels of seriousness of CKD. Risk of affliction of the disease increases with age and with the presence of certain risk factors including diabetes, high blood pressure and obesity, among others. While intervention with lifestyle changes including an improved diet and exercise can reduce the rate at which CKD progresses, there is no current treatment which will reverse the disease. Later stages of CKD lead to kidney failure which will require regular dialysis for the rest of the person's life or a kidney transplant.

The economic cost of CKD treatment is significant and largely correlated to stage of the disease. A study[12] by the U.S. Renal Data System found that 17% of Medicare spending goes to treatment of CKD. When including End Stage Renal Disease (ESRD), this figures increases to 24%. It further found that CKD patients incur, on average $23k of treatment costs compared to just $8k for non-CKD patients. Stage 4-5 patients incur yearly expenditures of almost $29k on average and hemodialysis patients expenses are nearly $90k annually. Total annual cost of CKD treatment in the U.S. is approximately $20 billion. Relative to reducing Medicare expenditures through improved treatment the authors suggest that, "…targeting the CKD population would have a large impact if improvements in care led to reduced comorbidities and hospitalizations."

Given the high cost of CKD treatment and lack of currently available treatments that can reverse the effects of CKD, if eventually developed and commercialized, we think a Cardiotoxin-based therapy could elicit significant interest from the clinical community.

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[11] Costa LA, Miles F, Diez RA, Araujo CE, Coni Molina CM and Cervellino JC*; Phase I study of VRCTC310, a purified phospholipase A2 purified from snake venom, in patients with refractory cancer: safety and pharmacokinetic data.* Anticancer Drugs 8 (9), 829-34 (Oct 1997)

[12] 2012 USRDS 2012 Annual Report. *Costs of Chronic Kidney Disease*

## IMMUNOPLEX

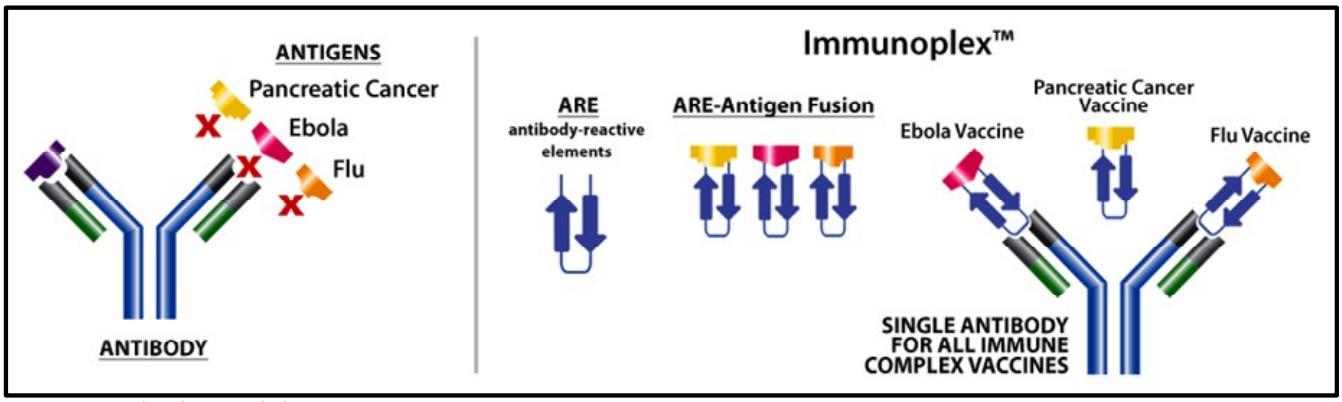
In June 2015 Spotlight acquired Memcine Pharmaceuticals, Inc., a biotechnology company located in the University of Iowa Research Park. Memcine has a platform technology called Immunoplex which is being developed to improve vaccine efficacy by using more efficient targeting and delivery. Immunoplex is in preclinical development for certain infectious diseases including influenza as well as for cancers of the breast, prostate and skin (melanoma).

Per terms of the transaction, STLT acquired 82% of the outstanding shares of Memcine for $25k. The agreement also calls for Spotlight to provide up to $3 million to help fund development of Immunoplex, which includes at least $150k by July 1, 2015 and another $150k by December 31, 2015. Tony Vanden Bush, PhD, co-founder of Memcine and co-inventor of the Immunoplex technology, was appointed as Chief Scientific Officer.

Memcine has publicly disclosed only limited information surrounding the components of the technology as well as the scope or outcomes of the conceptualized and/or completed preclinical studies. However, they do note that the heart of the technology is based on the use of a proprietary peptide tag which labels antigens and tumor cells of interest and to which a universal antibody binds to - this is what they term the "Immunoplex". The Immunoplex then delivers the antigen to immune cells and triggers a robust immune response.

The benefit of this technique compared to traditional vaccines, per Memcine, is that Immunoplex reduces exposure to potentially harmful adjuvants and can be delivered to mucosal surfaces without the use of needles. Some adjuvants have been linked to certain diseases in animal testing such as rheumatoid arthritis and cancer. And recently, controversy over certain adjuvants used in childhood vaccines and their potential association with autism has been a mainstream topic. In addition to lower exposure to adjuvants, Immunoplex also potentially significantly reduces the cost and time to develop a complex vaccine, which traditionally requires the identification and extensive testing of several antibodies.

**Immunoplex Technology**




SOURCE: Memcine Pharmaceuticals

The most recent development-related headline from Memcine was in July 2013 when they announced that researchers at the University of Iowa "expand(ed) animal testing of the Immunoplex technology as an immunotherapy for metastatic breast cancer." Memcine/Spotlight have not provided a recent update on further development timelines, although this may be upcoming now with the acquisition closed and additional funding potentially on the horizon.

Below is graphic from Memcine's website listing their current Immunoplex-related portfolio:

| Vaccine Candidate | State | Next Steps |
|---|---|---|
| Immunoplex™ HA flu | Proof-of-concept achieved in mice | License deal with partner |
| Immunoplex™ HepB | Proof-of-concept achieved in mice | License deal with partner |
| Immunoplex™ Ebola | Design Stage | Establish contract with USAAMRIID |
| Immunoplex™ Breast Cancer Immunotherapy | Early positive results in murine model | Dose-ranging and repeat-dose studies |
| Immunoplex™ Prostate Cancer Immunotherapy | Studies initiated | Dose-ranging and repeat-dose studies |
| Immunoplex™ Melanoma Immunotherapy | Model optimization | Initiate dose-ranging and repeat-dose studies |

## MILESTONES

**Grant Funding:** In June Celtic retained the FreeMind Group to seek public and private grant and contract funding opportunities to help fund development of the pipeline, including part 2 of the phase I crotoxin study. Freemind bills itself as "the premier international consulting firm specializing in assisting life science organizations secure non-dilutive funding from U.S. federal agencies and private foundations". Grant funding along with potential additional capital garnered through the capital markets and/or private transactions could help to accelerate product development in cancer, infectious disease and kidney disease.

**Portfolio Monetization:** Spotlight's specific strategy involves cultivating relationships with leading research universities and institutions, acquiring and further developing early-stage, high-potential technologies and then monetizing this through partnerships. We would expect that following further progress with development of lead projects including crotoxin for cancer, cardiotoxin for cancer and CKD and, potentially, crotamine as a PET radiopharmaceutical agent, that STLT will look for commercialization and/or licensing partners. These, however, may be more likely to materialize once the compounds reach at least a mid clinical-stage (i.e. phase 2) level of development. We also think there may be an earlier opportunity that could arise to partner and share some of the development cost and related risk.

**Crotoxin Phase I, Part 2:** Part 1 of the study was completed but Part 2 was subsequently suspended for reasons, per the notation on clinicaltrials.gov, related to "funding issues." However, per the company's August 24th press release, data from Part 1 of the study is now being aggregated and prepared for analysis with results potentially available in November. Spotlight is now making preparations to commence Part 2 of the study, which they think could commence early next year - the company recently engaged ImmunoClin, Inc., a contract research organization, to manage it.

Per Spotlight's July 21 press release announcing consummation of a Clinical Study Management Agreement with Immunoclin to manage the second part of the study, protocol of the second part may be amended from the original - details of which we think should be forthcoming. The press release did provide some detail on the second part including; expected enrollment of 12 patients at 3 sites in France, treatment duration is expected to be 37 days with 30-day follow-up and total duration of the study expected to be ~18 months. We think positive results from this phase 1 study would likely provide momentum to move to mid-stage studies and, possibly, attract interest from outside parties - which could potentially include investors and/or development/commercialization partners.

**Cardiotoxin CKD:** In March 2015 Celtic announced that they in-licensed worldwide (ex-China) rights to develop and market Cardiotoxin for the treatment of CKD. As there are currently no available treatments that can reverse the effects of CKD, if eventually developed and commercialized, we think a Cardiotoxin-based therapy could elicit significant interest from the clinical community.

Positive preclinical study data demonstrating cardiotoxin's ability to reduce the effects of CKD were published in April 2014. STLT/Celtic have indicated that they plan to move directly to clinical trials and note in their Q1 10-Q that, "Clinical trials are expected to be relatively straightforward to organize and the clinical endpoints well established. A small trial could be completed to establish the baseline response prior to committing to full scale

studies. We could see studies well underway before 2015 year end with the FDA trial wrapped up by the end of fiscal 2016."

**Crotamine:** Celtic is looking to further beef up their snake venom-based pipeline and recently consummated a deal to acquire rights to crotamine from Instituto Butantan. Butantan is the largest biopharmaceutical organization in Brazil which has done extensive research on crotamine, a cell-penetrating peptide derived from rattlesnake venom. Studies have shown that crotamine has the unique properties of being both cell penetrating and possessing antimicrobial activities and selectively targets certain proliferating cells. These characteristics have sparked interest in crotamine as both a labeling agent for highly replicating cells (for applications such as a radiopharmaceutical agent) and for use in chemotherapy applications.[13]

In July 2015 STLT announced an agreement between Celtic and Emory University whereby Emory will design and conduct a phase I study for use of crotamine as a PET radiopharmaceutical imaging agent for lung cancer. We expect to hear more specifics relative to the study design in the future.

**EPISORB:** In March/April 2015 STLT announced that Celtic launched EPISROB, a topical gel that will be sold to compounding pharmacies for use as a transdermal drug delivery agent with analgesic and scar reduction creams. STLT/Celtic have not disclosed the active ingredient in EPISORB but note in their April 6th press release that the "product makes use of the attributes of cardiotoxin as a cell penetrating peptide." The companies are also considering a formulation to be used in the treatment of precancerous skin lesions. EPISORB has been registered with FDA and is listed in the Pharmacy Benefit Managers database which is used by third party payors for reimbursement purposes. While we think EPISORB is not likely to generate significant revenue for STLT, launch of the product is a meaningful milestone as it marks the company's first product on the market.

**Additional Financing:** Cash balance at June 30th was $1.0 million (in addition to $120k in restricted cash) which was bolstered by the sale of $1.7 million (net) of convertible notes during Q1. Cash burn has been fairly moderate in the past with just $986k used (ex changes in working capital) through the first six months of this year and $1.3 million used in all of fiscal 2014. We expect the company will be looking to raise additional capital in the near term for general operating activities and to use to advance their product pipeline.

| **Current Debt** | | |
|---|---|---|
| Notes Payable | $353,631 | Inherited from American Exploration, which STLT was reversed merged with. Notes are due on demand and not in default |
| Credit Line | $886,693 | Due on demand. Not in default. Total credit borrowing limit is $1.002M |
| Related party debt | $166,410 | Portion of this is past due |
| Convertible debt | $923,600 | Portion in default. Convertible into common shares |
| TOTAL | **$2,330,334** | |

[13] Radis-Baptista G, Kerkis I. Crotamine, *A Small Basic Polypetdie Myotoxin From Rattlesnake Venom with Cell-Penetrating Properties*. Current Pharmaceutical Design. 2011 Dec;17(38):4351-61

## VALUATION / RECOMMENDATION

Given the pre-revenue stage of Spotlight, typical valuation methodologies such as P/E, P/EG, P/S and others which require financial metrics as components are unsuitable. As such, we believe the most appropriate valuation methodology is to compare STLT to other pre- (and very early) revenue stage companies focused on cancer therapeutics. Our list below does not include any that are involved with venom-based cancer therapeutics as there are none that we were able to find which are publicly traded and solely or almost entirely focused on that area. We note that most venom-based research is housed at academic institutions, private companies or very large, multi-disciplinary publicly traded companies - none of which are appropriate comps for STLT.

So we think our comparable cohort is a fair representation of mostly pure-play oncology-related therapy companies at various stages of development. We use a comparable enterprise value (EV) by ranking the development phase of each of the companies' main product candidates. Lowest ranking (1) is associated with preclinical stage while highest ranking (4) is associated with phase 3 clinical testing stage. See our "Key" for specifics of each rating's association to their respective development phase.

Average EV and development phase rating of the 13 comparable companies is $34 million and 3.0, respectively. Which equates to $11.3 million (= $34M / 3.0) of EV for each development stage. As STLT is in the preclinical to phase I stage, we assign an EV of approximately $23 million (= 2 x $11.3M), which equates to a market value of approximately $22 million or ~ $1.70/share.

The shares are very thinly traded and have priced at between $1.05 and $1.39 since about mid-May. Float is listed at approxmately 45% of o/s shares (6.1M of 13.8M). Our calculated fair value implies some upside in the most recent quoted price although the extremely low volume creates inherent risk of mispricing and potential difficulty in publicly exiting an investment. We are maintaining our Hold recommendation.

Considerations for an upgrade include substantive progress of candidates through development as well as a more comfortable level of operating capital.

| Company | Tkr | EV (M) | Dvlpmt Phase | Dvlpmt Ph Rating |
|---|---|---|---|---|
| OXIS International Inc | OXIS | $12 | Preclinical | 1 |
| Cellectar Biosciences Inc | CLRB | $17 | Phase 1/2 | 2.5 |
| OncoVista Innovative Therapies | OVIT | $17 | Phase 1/2 | 2.5 |
| Del Mar Pharmaceuticals Inc | DMPI | $18 | Phase 1/2 | 2.5 |
| TapImmune Inc | TPIV | $18 | Phase 2 | 3 |
| Sioligenix Inc | SNGX | $42 | Phase 2 | 3 |
| Bio-Path Holdings Inc | BPTH | $96 | Phase 2 | 3 |
| ImmunoCellular Therapeutics Ltd | IMUC | $9 | Phase 2 | 3 |
| OncoSec Medical Inc | ONCS | $53 | Phase 2 | 3 |
| CASI Pharmaceuticals Inc | CASI | $45 | Ph 1 thru 3 | 3 |
| DanDrit Biotech | DDRT | $44 | Phase 3 | 4 |
| Celator Pharmaceuticals | CPXX | $55 | Phase 3 | 4 |
| Onconova Therapeutics Inc | ONTX | $16 | Phase 3 | 4 |
| **Average** | | **$34** | | **3.0** |

| KEY: | | |
|---|---|---|
| **Development Phase** | equates to | **Development Rating** |
| Preclinical | | 1 |
| Phase 1 | | 2 |
| Phase 1/2 | | 2.5 |
| Phase 2 | | 3 |
| Phase 3 | | 4 |

## FINANCIAL MODEL

Spotlight Innovation, Inc.

| | 2014 A | Q1A | Q2A | Q3E | Q4E | 2015 E | 2016 E |
|---|---|---|---|---|---|---|---|
| Total Revenues | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 |
| *YOY Growth* | - | - | - | - | - | - | - |
| COGS | $0.0 | $0.00 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 |
| Gross Income | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 |
| *Gross Margin* | - | - | - | - | - | - | - |
| SG&A | $1,486.6 | $649.5 | $733.6 | $682.0 | $769.5 | $2,834.6 | $3,132.0 |
| *% SG&A* | - | - | - | - | - | - | - |
| R&D | $0.0 | $0.0 | $3.7 | $6.2 | $14.5 | $24.4 | $318.0 |
| *% R&D* | *#DIV/0!* | - | - | - | - | - | - |
| Operating Income | ($1,486.6) | ($649.5) | ($737.2) | ($688.2) | ($784.0) | ($2,859.0) | ($3,450.0) |
| *Operating Margin* | - | - | - | - | - | - | - |
| Total Other Income (Expense) | ($2,138.6) | ($311.8) | ($265.8) | ($318.0) | ($384.0) | ($1,279.9) | ($2,128.0) |
| Pre-Tax Income | ($3,625.3) | ($961.3) | ($1,003.0) | ($1,006.2) | ($1,168.0) | ($4,138.9) | ($5,578.0) |
| Tax expense (benefit) | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 |
| *Tax Rate* | *0.0%* | *0.0%* | *0.0%* | *0.0%* | *0.0%* | *0.0%* | *0.0%* |
| Preferred dividends | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 |
| Income to non-contrl interest | -$1.8 | $0.2 | -$1.3 | $0.0 | $0.0 | -$1.0 | $0.0 |
| Net Income | ($3,623.5) | ($961.6) | ($1,001.8) | ($1,006.2) | ($1,168.0) | ($4,137.9) | ($5,578.0) |
| *YOY Growth* | *-46.8%* | *751.8%* | *-12.7%* | *31.3%* | *-26.8%* | *14.2%* | *34.8%* |
| *Net Margin* | - | - | - | - | - | - | - |
| EPS | ($0.28) | ($0.07) | ($0.07) | ($0.07) | ($0.08) | ($0.30) | ($0.28) |
| *YOY Growth* | *-71.0%* | | | | | *6.4%* | *-4.0%* |
| Diluted Shares O/S | 13,007 | 13,413 | 13,742 | 14,220 | 14,455 | 13,957 | 19,600 |

*Brian Marckx, CFA*

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## LEADERSHIP

**Cristopher Grunewald**
***Chief Executive Officer***
Mr. Grunewald is a financial executive and entrepreneur with background in the healthcare and biotechnology sectors, private equity and investment banking. He has been involved in all stages of the commercialization of healthcare IP developed by premiere research and development institutions.

**Dr. David Hostelley**
***Chief Financial Officer***
Dr. Hostelley has twenty years as a consultant in the health field, and has served as CEO, CFO and board member of several publicly traded companies. Dr. Hostelley is a CPA (inactive) licensed by the state of Ohio. He earned his Ph.D. in management while a lecturer in the MBA Program of Baldwin-Wallace College, and has lectured in Accounting and Management for Walsh University, North Canton, Ohio.

**Jeffrey Stein, Esq.**
***Securities Counsel***
Mr. Stein serves as securities counsel for Spotlight Innovation. He has over fifteen years of experience providing high quality, personalized attention to public companies, including more than thirty reverse mergers, IPOs and APOs.

**Rene Erickson**
***Corporate Communications***
Mr. Erickson has three decades of corporate communications experience across diverse industries including healthcare, information technology, aviation and academia.

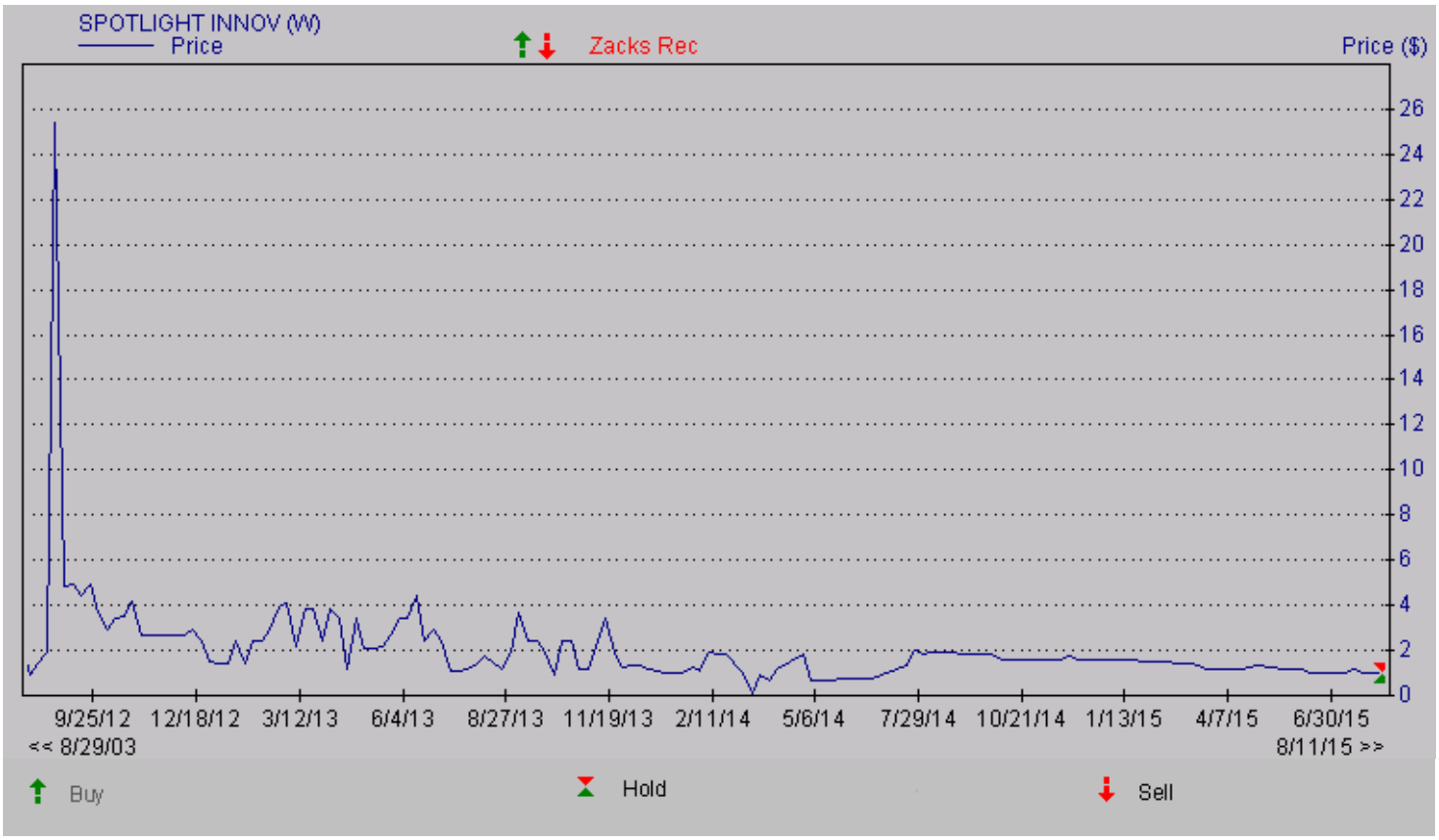
**Mike Reysack**
***University Partnerships***
Mr. Reysack leads University Partnerships for Spotlight Innovation. He has extensive experience cultivating and managing relationships with stakeholders, including fifteen years as an consultant and business strategist for venture and early stage companies, providing effective communications between companies and the financial community.

**Dr. Paul F. Reid**
***President and Director of Celtic Biotech***
Dr. Reid has extensive experience in drug production, new drug development, clinical trial design, and experimental design. His collaborations with Harvard University Professor Zheng Hong Qin have led to several patent applications in relation to proprietary compounds, and publication of a number of articles in peer reviewed international publications. Dr. Reid is widely experienced in medical regulatory affairs and FDA protocols.

**Tony Vanden Bush, PhD**
***Co-Founder, Co-Inventor, Director and Chief Scientific Officer of Memcine Pharmaceuticals***
Tony is a research scientist in the University of Iowa department of Microbiology. Prior to forming Memcine Pharmaceuticals, Dr. Vanden Bush conducted research at the Veterans Association Medical Center in Iowa City, IA. Dr. Vanden Bush also serves on the scientific advisory board for Memcine. Dr. Vanden Bush has an undergraduate degree in Biochemistry/Molecular Biology from University of Wisconsin, Eau Claire, and a PhD with honors in Immunobiology and a graduate minor in Biochemistry from Iowa State University.

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## HISTORICAL ZACKS RECOMMENDATIONS



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