

Celsion CORP
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**Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-206789**

PROSPECTUS SUPPLEMENT

(To Prospectus dated September 25, 2015)

5,142,857 Shares of Common Stock

Pursuant to this prospectus supplement and the accompanying prospectus (the “accompanying prospectus”), we are offering 5,142,857 shares of our common stock, par value \$0.01 per share, to several investors at an offering price of \$0.35 per share for an aggregate purchase price of \$1,800,000. In a concurrent private placement, we are selling to each purchaser, for each share of common stock purchased in this offering, a warrant to purchase a share of common stock. The warrants have an exercise price of \$0.46 per share, are initially exercisable six months following issuance, and terminate five and one-half years following issuance. The warrants and the shares of our common stock issuable upon exercise of the warrants are not being registered under the Securities Act of 1933, as amended (the “Securities Act”), are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being sold pursuant to the exemption provided in Section 4(a)(2) under the Securities Act and Rule 506(b) promulgated thereunder.

Our common stock is listed on The NASDAQ Capital Market under the symbol “CLSN.” On December 20, 2016, the last reported sale price of our common stock on The NASDAQ Capital Market was \$0.35 per share.

As of December 20, 2016, the aggregate market value of our voting and non-voting common stock held by non-affiliates pursuant to General Instruction I.B.6. of Form S-3 was \$29,767,714 which was calculated based on 25,661,822 outstanding shares of our voting and non-voting common stock held by non-affiliates and at a price of \$1.16 per share, the closing sale price of our common stock reported on The NASDAQ Capital Market on October 21, 2016. As a result, we are eligible to offer and sell up to an aggregate of \$3,145,571 of shares of our common stock pursuant to General Instruction I.B.6. of Form S-3. Following this offering, we will have sold securities with an aggregate market value of \$8,576,919 pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on, and includes, the date of this prospectus supplement.

As of the date of this prospectus supplement, an aggregate of \$65,850,708 of shares of common stock and other securities remain unsold under the registration statement on Form S-3 (File No. 333-206789) we filed with the Securities and Exchange Commission on September 4, 2015 and declared effective on September 25, 2015.

Pursuant to the Controlled Equity OfferingSM Sales Agreement dated as of February 1, 2013 (the “Sales Agreement”), by and between Cantor Fitzgerald & Co. and us, we may offer and sell, from time to time through “at-the-market” offerings, up to an aggregate of \$25.0 million of shares of our common stock. We filed with the Securities and Exchange Commission a prospectus supplement dated October 2, 2015 to the accompanying prospectus, covering the sales of shares of our common stock under the Sales Agreement. We have sold shares of our common stock under the Sales Agreement generating total gross proceeds of approximately \$7.6 million and have up to approximately \$17.4 million available for future sale under the Sales Agreement. In connection with this offering, we have agreed not to sell any additional shares under the Sales Agreement until the six-month anniversary of the closing date of this offering.

Investing in our securities involves a high degree of risk. Before making an investment decision, please read “Risk Factors” beginning on page S-11 of this prospectus supplement, page 9 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

We are selling the shares of common stock offered hereby directly to several investors. We have retained H.C. Wainwright & Co., LLC to act as our exclusive placement agent in connection with this offering. The placement agent has agreed to use its reasonable best efforts to solicit offers to purchase our common stock. We have agreed to pay the placement agent a fee of 6.5% of the aggregate gross proceeds in this offering. The placement agent is not purchasing or selling any shares of our common stock pursuant to this prospectus supplement or the accompanying prospectus, nor are we requiring any minimum purchase or sale of any specific number of shares of our common stock. See “Plan of Distribution” beginning on page S-29 of this prospectus supplement for more information regarding these arrangements.

	Public Offering Price	Placement Agent Fee⁽¹⁾	Proceeds, before expenses, to us
Per Common Stock	\$0.3500	\$ 0.02275	\$0.32725
Total For All Shares	\$ 1,800,000	\$ 117,000	\$ 1,683,000

In addition to the placement agent fees, we have agreed to reimburse the placement agent in the amount of \$25,000 for its legal fees and expenses in connection with this offering and up to \$10,000 for its other out-of-pocket expenses in connection with this offering. See “Plan of Distribution” beginning on page S-29 of this prospectus supplement for more information.

Delivery of the shares of common stock will take place on or about December 23, 2016, subject to the satisfaction of certain conditions.

Exclusive Placement Agent

Rodman & Renshaw

A unit of H.C. Wainwright & Co.

The date of this prospectus supplement is December 20, 2016

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a “shelf” registration statement on Form S-3 (File No. 333-206789) that we filed with the Securities and Exchange Commission on September 4, 2015 and declared effective on September 25, 2015.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which gives more general information about the shares of our common stock and other securities we may offer from time to time under our shelf registration statement, some of which does not apply to the securities offered by this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference herein or therein, on the other hand, you should rely on the information in this prospectus supplement.

You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering before making an investment decision. You should also read and consider the information in the documents referred to in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.”

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it.

We are not making an offer to sell the securities covered by this prospectus supplement in any jurisdiction where the offer or sale is not permitted.

The information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of its respective date, regardless of the time of delivery of the respective document or of any sale of securities covered by this prospectus supplement. You should not assume that the information contained in or incorporated by reference in this prospectus supplement or the accompanying prospectus, or in any free writing prospectus that we have authorized for use in connection with this

offering, is accurate as of any date other than the respective dates thereof.

Unless the context indicates otherwise, as used in this prospectus, the terms “Celsion,” “the Company,” “we,” “us” and “our” refer to Celsion Corporation, a Delaware corporation, and its wholly-owned subsidiary CLSN Laboratories, Inc., also a Delaware corporation. The Celsion brand and product names, including but not limited to Celsion®, ThermoDox®, EGEN®, TheraPlas™ and TheraSilence™ contained in this prospectus are trademarks, registered trademarks or service marks of Celsion Corporation or its subsidiary in the United States and certain other countries. This document may also contain references to trademarks and service marks of other companies that are the property of their respective owners.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in the securities covered by this prospectus supplement. For a more complete understanding of Celsion and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information set forth in the section titled “Risk Factors” in this prospectus supplement beginning on page S-11.

Overview

Celsion is a fully-integrated oncology drug development stage company focused on developing a portfolio of innovative cancer treatments, including directed chemotherapies, DNA-mediated immunotherapy and RNA based therapies. Our lead product candidate is ThermoDox®, a proprietary dosage form of doxorubicin based on a heat-activated liposomal platform technology, currently in Phase III development for the treatment of primary liver cancer. Our pipeline also includes GEN-1, a DNA-based immunotherapy in clinical development for the localized treatment of ovarian cancer and pre-clinical development for brain cancer. GEN-1 is based on a platform technology for the development of treatments for those suffering with difficult-to-treat forms of cancer, using novel nucleic acid-based immunotherapies and other anti-cancer DNA or RNA therapies. We are working to develop and commercialize more efficient, effective and targeted oncology therapies based on our technologies, with the goal of developing novel therapeutics that maximize efficacy while minimizing side-effects common to cancer treatments.

ThermoDox®

ThermoDox® is being evaluated in a Phase III clinical trial, in combination with a standardized radiofrequency ablation (“RFA”), for primary liver cancer (the “OPTIMA Study”) and a Phase II clinical trial for recurrent chest wall breast cancer (the “DIGNITY Study”). ThermoDox® is a liposomal encapsulation of doxorubicin, an approved and frequently used oncology drug for the treatment of a wide range of cancers. Localized heat at hyperthermia temperatures (greater than 40 degrees Celsius) releases the encapsulated doxorubicin from the liposome enabling high concentrations of doxorubicin to be deposited preferentially in and around the targeted tumor.

The OPTIMA Study

On February 24, 2014, we announced that the United States Food and Drug Administration (the “FDA”), after its customary 30-day review period, provided clearance for the OPTIMA Study, which is a pivotal, double-blind, placebo-controlled Phase III trial of ThermoDox®, in combination with standardized RFA, for the treatment of primary liver cancer. The trial design of the OPTIMA Study is based on the comprehensive analysis of data from an earlier clinical trial called the HEAT Study, which is described below. We launched the OPTIMA Study in the first half of 2014. The OPTIMA Study was designed with extensive input from globally recognized hepatocellular carcinoma (“HCC”) researchers and clinicians and after receiving formal written consultation from the FDA. The OPTIMA Study is expected to enroll up to 550 patients globally at up to 75 sites in the United States, Canada, Europe, China and other Asia Pacific countries, and will evaluate ThermoDox® in combination with standardized RFA, which will require a minimum of 45 minutes across all investigators and clinical sites for treating lesions three to seven centimeters, versus standardized RFA alone. The primary endpoint for this clinical trial is overall survival (“OS”), and the secondary endpoints are progression free survival and safety. The statistical plan calls for two interim efficacy analyses by an independent Data Monitoring Committee.

On December 16, 2015, we announced that we had received the clinical trial application approval from the China Food and Drug Administration (the “CFDA”) to conduct the OPTIMA Study in China. This clinical trial application approval will now allow Celsion to enroll patients at up to 20 additional clinical sites in China. With the addition of these Chinese clinical sites, we expect to complete enrollment in the OPTIMA Study during the first half of 2018. On April 26, 2016, we announced that the first patient in China has been enrolled in the OPTIMA Study. Results from the OPTIMA Study, if successful, will provide the basis for a global registration filing and marketing approval.

The OPTIMA Study represents an evaluation of ThermoDox® in combination with a first line therapy, RFA, for newly diagnosed, intermediate stage HCC patients. HCC incidence globally is approximately 850,000 new cases. The RFA addressable percentage of the newly diagnosed patients is approximately 30%. The OPTIMA Study is supported with a convincing hypothesis developed from an overall survival analysis of a large subgroup of patients from the HEAT Study.

Findings from the HEAT Study post-hoc data analysis suggest that ThermoDox® may substantially improve OS, when compared to the control group, in patients if their lesions undergo a 45 minute RFA procedure standardized for a lesion greater than 3 cm in diameter. Data from nine OS sweeps have been conducted since the top line progression free survival (“PFS”) data from the HEAT Study were announced in January 2013, with each data set demonstrating progressive improvement in clinical benefit and statistical significance. On August 15, 2016, we announced updated results from its final retrospective OS analysis of the data from the HEAT Study. These results demonstrated that in a large, well bounded, subgroup of patients with a single lesion (n=285, 41% of the HEAT Study patients), treatment with a combination of ThermoDox® and optimized RFA provided an average 54% risk improvement in OS compared to optimized RFA alone. The Hazard Ratio (“HR”) at this analysis is 0.65 (95% CI 0.45 - 0.94) with a p-value of 0.02. Median OS for the ThermoDox® group has been reached which translates into a two year survival benefit over the optimized RFA group (projected to be greater than 80 months for the ThermoDox® plus optimized RFA group compared to less than 60 months projection for the optimized RFA only group). Additional findings from this most recent analysis specific to the Chinese patient cohort of 223 patients are summarized below:

In the population of 154 patients with a single lesion (70% of the HEAT Study Chinese patient cohort) who received optimized RFA treatment for 45 minutes or more showed a 53% risk improvement in OS (HR = 0.66) when treated with ThermoDox® plus optimized RFA.

These data continue to support and further strengthen ThermoDox®'s potential to significantly improve OS compared to an RFA control in patients with lesions that undergo optimized RFA treatment for 45 minutes or more. The clinical benefit seen in the ITT Chinese patient cohort further confirms the importance of RFA heating time as 72% of patients in this large patient cohort in China received an optimized RFA treatment.

While this information should be viewed with caution since it is based on a retrospective analysis of a subgroup, we also conducted additional analysis that further strengthens the evidence for the HEAT Study sub-group. We commissioned an independent computational model at the University of South Carolina Medical School. The results unequivocally indicate that longer RFA heating times correlate with significant increases in doxorubicin concentration around the RFA treated tissue. We conducted a prospective preclinical study in a 21 pigs using two different manufacturers of RFA and human equivalent doses of ThermoDox® that clearly support the relationship between increased heating duration and clinical outcomes.

On November 29, 2016, we announced the presentation of results from an independent analysis conducted by the National Institutes of Health (the “NIH”) from the HEAT Study which reaffirmed the correlation between increased RFA burn time per tumor volume and improvements in overall survival. The NIH analysis, which sought to evaluate the correlation between RFA burn time per tumor volume (min/ml) and clinical outcome, concluded that increased burn time per tumor volume significantly improved overall survival in patients treated with RFA and ThermoDox® compared to patients treated with RFA alone.

The HEAT Study

On January 31, 2013, we announced that the HEAT Study, ThermoDox® in combination with RFA, did not meet the primary endpoint, PFS, of a Phase III clinical trial enrolling 701 patients with primary liver cancer. This determination was made after conferring with the HEAT Study independent Data Monitoring Committee, that the HEAT Study did not meet the goal of demonstrating a clinically meaningful improvement in progression free survival. In the trial, ThermoDox® was well-tolerated with no unexpected serious adverse events. Following the announcement of the HEAT Study results, we followed patients for OS, the secondary endpoint of the HEAT Study. We have conducted a comprehensive analysis of the data from the HEAT Study to assess the future strategic value and development strategy for ThermoDox®.

The DIGNITY Study

On December 14, 2015, we announced final data from our ongoing DIGNITY study, which is an open-label, dose-escalating Phase II trial of ThermoDox® in patients with recurrent chest wall (“RCW”) breast cancer. The DIGNITY Study is designed to establish a safe therapeutic dose in Phase I, and in Phase II to demonstrate local control, including complete and partial responses, and stable disease as its primary endpoint. The DIGNITY Study is also planned to evaluate kinetics in ThermoDox® produced from more than one manufacturing site. Of the 28 patients enrolled and treated, 21 patients were eligible for evaluation of efficacy. Approximately 62% of evaluable patients experienced a local response, including six complete responses and seven partial responses.

The Euro-DIGNITY Study

We anticipate that a Phase II study of RadioTherapy, HyperThermia and ThermoDox® to treat patients with local-regional recurrent chest wall breast cancer will be initiated by four to five clinical sites located in Italy, Israel, Poland and the Czech Republic (the “Euro-DIGNITY Study”). The Euro-DIGNITY Study is expected to commence in 2017 and should enroll up to 70 patients affected by recurrent breast adenocarcinoma on the chest wall with/without nodes over a period of two years.

The primary objectives of the Euro-DIGNITY Study will be (i) to evaluate efficacy in patients after 3 cycles of ThermoDox® plus Hyperthermia measuring tumor diameter as a response to therapy and (ii) to evaluate loco-regional breast tumor control in patients who undergo ThermoDox®/hyperthermia/radiotherapy as measured by target lesion clinical response rate combining a RECIST criteria with digital photography to gauge response.

Secondary objectives of the Euro-DIGNITY Study will be (i) to evaluate the safety of the combination of ThermoDox/Hyperthermia/Radiotherapy among patients with local-regional recurrence (“LRR”) breast cancer, (ii) to evaluate the duration of local control complete response, partial response and stable disease following treatment with ThermoDox/Hyperthermia/Radiotherapy up to 24 months among patients with LRR breast cancer and (iii) to assess Patient Reported Quality of Life using the FACT-B and Brief Pain Inventory following treatment with ThermoDox/Hyperthermia/Radiotherapy among patients with LRR breast cancer.

Acquisition of EGEN Assets

On June 20, 2014, we completed the acquisition of substantially all of the assets of Egen, Inc., an Alabama corporation, which has changed its company name to EGWU, Inc. after the closing of the acquisition (“EGEN”), pursuant to an asset purchase agreement dated as of June 6, 2014, by and between EGEN and Celsion (the purchase agreement). We acquired all of EGEN’s right, title and interest in and to substantially all of the assets of EGEN, including cash and cash equivalents, patents, trademarks and other intellectual property rights, clinical data, certain contracts, licenses and permits, equipment, furniture, office equipment, furnishings, supplies and other tangible personal property. In addition, CLSN Laboratories assumed certain specified liabilities of EGEN, including the liabilities arising out of the acquired contracts and other assets relating to periods after the closing date.

The total purchase price for the asset acquisition is up to \$44.4 million, including potential future earnout payments of up to \$30.4 million contingent upon achievement of certain earnout milestones set forth in the purchase agreement. At the closing, we paid approximately \$3.0 million in cash after the expense adjustment and issued 2,712,188 shares of our common stock to EGEN. The shares of common stock were issued in a private transaction exempt from registration under the Securities Act, pursuant to Section 4(a)(2) thereof. In addition, 670,070 shares of common stock

were held back by us at the closing and are issuable to EGEN on or after August 2, 2016 pending certain potential adjustments for expenses or in relation to EGEN's indemnification obligations under the purchase agreement.

The earnout payments of up to \$30.4 million will become payable, in cash, shares of our common stock or a combination thereof, at our option, as follows:

\$12.4 million will become payable upon achieving certain specified development milestones relating to an ovarian cancer study of GEN-1 (formerly known as EGEN-001) to be conducted by us or our subsidiary;

\$12.0 million will become payable upon achieving certain specified development milestones relating to a GEN-1 glioblastoma multiforme brain cancer study to be conducted by us or our subsidiary; and

up to \$6.0 million will become payable upon achieving certain specified milestones relating to the TheraSilence™ technology acquired from EGEN in the acquisition.

Our obligations to make the earnout payments will terminate on the seventh anniversary of the closing date.

In the acquisition, we purchased GEN-1 (formerly known as EGEN-001), a DNA-based immunotherapy for the localized treatment of ovarian and brain cancers, and three platform technologies for the development of treatments for those suffering with difficult-to-treat forms of cancer, novel nucleic acid-based immunotherapies and other anti-cancer DNA or RNA therapies, including TheraPlas™ and TheraSilence™.

GEN-1

GEN-1 is a DNA-based immunotherapeutic product for the localized treatment of ovarian and brain cancers by intraperitoneally administering an Interleukin-12 (“IL-12”) plasmid formulated with our proprietary TheraPlas™ delivery system. In this DNA-based approach, the immunotherapy is combined with a standard chemotherapy drug, which can potentially achieve better clinical outcomes than with chemotherapy alone. We believe that increases in IL-12 concentrations at tumor sites for several days after a single administration could create a potent immune environment against tumor activity and that a direct killing of the tumor with concomitant use of cytotoxic chemotherapy could result in a more robust and durable antitumor response than chemotherapy alone.

GEN-1 OVATION Study.

In February 2015, we announced that the FDA accepted, without objection, the Phase I dose-escalation clinical trial of GEN-1 in combination with the standard of care in neo-adjuvant ovarian cancer (the “OVATION Study”). On September 30, 2015, we announced enrollment of the first patient in the OVATION Study. The OVATION Study will seek to identify a safe, tolerable and potentially therapeutically active dose of GEN-1 by recruiting and maximizing an immune response and is designed to enroll three to six patients per dose level and will evaluate safety and efficacy and attempt to define an optimal dose for a follow-on Phase I/II study combining GEN-1 with Avastin® and Doxil®. In addition, the OVATION Study establishes a unique opportunity to assess how cytokine-based compounds such as GEN-1, directly affect ovarian cancer cells and the tumor microenvironment in newly diagnosed patients. The study is designed to characterize the nature of the immune response triggered by GEN-1 at various levels of the patients' immune system, including:

infiltration of cancer fighting T-cell lymphocytes into primary tumor and tumor microenvironment including peritoneal cavity, which is the primary site of metastasis of ovarian cancer;

changes in local and systemic levels of immuno-stimulatory and immunosuppressive cytokines associated with tumor suppression and growth, respectively; and

expression profile of a comprehensive panel of immune related genes in pre-treatment and GEN-1-treated tumor tissue.

We have initiated the OVATION Study at four clinical sites at the University of Alabama at Birmingham, Oklahoma University Medical Center, Washington University in St. Louis and the Medical College of Wisconsin. In February 2016, we announced the completion of enrollment of the first cohort of patients in the OVATION Study. The OVATION Study will continue into 2016 at higher doses of GEN-1 with the goal to identify a safe, tolerable and therapeutically active dose of GEN-1 by recruiting and maximizing an immune response.

During 2016, we announced data from the first three cohorts of patients in the OVATION Study, respectively. The OVATION Study is designed to enroll three to six patients per dose cohort and will continue into 2016 at higher doses of GEN-1 with the goal to identify a safe, tolerable and therapeutically active dose of GEN-1 by recruiting and maximizing an immune response. The first three cohorts each enrolled three patients. Enrollment in the fourth cohort is ongoing, and Celsion expects to complete the OVATION Study in the first half of 2017. Future studies of GEN-1 will include a Phase I/II study combining GEN-1 with Avastin® and Doxil®. The results of the OVATION Study to date are as follows:

Totality of Results in the First Three Cohorts

Of the first nine patients dosed, one patient demonstrated a complete response (“CR”), five patients demonstrated partial response (“PR”) and three patients demonstrated stable disease (“SD”), as measured by RECIST criteria. This translates to a 100% disease control rate (“DCR”) and 66% objective response rate (“ORR”).

Eight patients had successful resections of their tumors, with four patients having an R0 resection, which indicates a microscopically margin-negative resection in which no gross or microscopic tumor remains in the tumor bed, and three patients with a R1 resection, indicating microscopic residual tumor. One patient had an R2, indicating macroscopic residual tumor. One patient in the second cohort was ineligible for debulking surgery due to a medical complication unrelated to the study or the study drug.

Of the eight surgically treated and evaluable patients, one patient demonstrated a complete pathological response (“cPR”), three patients demonstrated a micro pathological response (“microPR”), and four patients demonstrated a macroPR. These data compare favorably to historical data, which indicate that cPRs are typically seen in less than 7% of patients receiving neoadjuvant chemotherapy followed by surgical resection. cPRs have been associated with a median overall survival of 72 months, which is more than three years longer than those who do not experience a cPR. In addition, microPRs are seen in approximately 30% of patients, and are associated with a median overall survival of 38 months.

Seven patients who completed treatment follow-up experienced a dramatic (greater than 90%) drop in their CA-125 protein levels as of their most recent study visit. CA-125 is used to monitor certain cancers during and after treatment. CA-125 is present in greater concentrations in ovarian cancer cells than in other cells. A 50% reduction in CA-125 levels is considered meaningful. Six patients maintained CA-125 levels below the standard cutoff level of 35 U/mL.

Top Line Translational Data from First Two Cohorts

Celsion also reported initial translational data from the first two cohorts of patients. Tumor and blood samples collected before the start of the neoadjuvant chemotherapy (“NACT”) and after the completion of GEN-1 treatment at debulking surgery are being analyzed for immune cell populations. Top line data demonstrates intriguing immunological changes in the tumor that are consistent with the activation of the immune system. Specifically,

In tumor tissue, there was an increase in cytotoxic CD8+ T-cell density in three out of four evaluable patients at debulking surgery. There was a decrease in immunosuppressive FoxP3+ T-cells in two out of those 4 patients. The ratio of CD8+/FoxP3+ cells was increased in all four evaluable patients. High tumor infiltrating CD8+ T-cell density, low FoxP3+ T-cell density or high CD8+/FoxP3+ ratio demonstrate a potential shift in tumor environment to favoring immune stimulation following NACT + GEN-1 therapy. For the remaining two patients the post-treatment tumor tissue was not available. In one of those two patients there was complete pathological response hence no tumor tissue was present to provide a post-treatment comparison. In the other patient the debulking surgery was not performed due to disease related complications.

In plasma samples, there appeared to be no significant change in T-cell density following the treatment. The density of myeloid derived suppressor cells that are associated with immunosuppression in ovarian cancer were either decreased or did not increase in post-treatment samples.

Additional immune analysis of biological tissue including cytokine ELISA from the first two patient cohorts and a complete analysis of the two higher dose cohorts is in progress.

GEN-1 Plus Doxil[®] and Avastin[®] Trial.

On April 29, 2015, we announced the expansion of our ovarian cancer development program to include a Phase I dose escalating trial to evaluate GEN-1 in combination with Avastin[®] and Doxil[®] in platinum-resistant ovarian cancer patients. We expect to enroll patients beginning in 2017. This new combination study in platinum-resistant ovarian cancer is supported by three preclinical studies indicating that the combination of GEN-1 with Avastin[®] may result in significant clinical benefit with a favorable safety profile. Specifically:

In two preclinical studies using an animal model of disseminated ovarian cancer, GEN-1 in combination with Avastin® led to a significant reduction in tumor burden and disease progression. The effectiveness of the combined treatment was seen when GEN-1 was combined with various dose levels of Avastin® (low-medium-high). Additionally, it was shown that GEN-1 treatment alone resulted in anti-tumor activity that was as good as or better than Avastin® treatment alone.

The preclinical studies indicated that no obvious overt toxicities were associated with the combined treatments. The preclinical data are also consistent with the mechanism of action for GEN-1, which exhibits certain anti-angiogenic properties and suggests that combining GEN-1 with lower doses of Avastin® may enhance efficacy and help reduce the known toxicities associated with this anti-VEGF drug.

The distinct biological activities of GEN-1 (immune stimulation) and Avastin® (inhibition of tumor blood vessel formation) makes a sound scientific rationale for this combination approach. Additionally, the anti-angiogenic activity of GEN-1 mediated through up regulation of the interferon gamma (“IFN-g”) pathway may help to explain the remarkable synergy between GEN-1 and Avastin® and potentially addresses the VEGF escape mechanisms associated with resistance to Avastin® therapy.

TheraPlas™ Technology Platform

TheraPlas™ is a technology platform for the delivery of DNA and messenger RNA (“mRNA”) therapeutics via synthetic non-viral carriers and is capable of providing cell transfection for double-stranded DNA plasmids and large therapeutic RNA segments such as mRNA. There are two components of the TheraPlas™ system, a plasmid DNA or mRNA payload encoding a therapeutic protein and a delivery system. The delivery system is designed to protect the DNA/RNA from degradation and promote trafficking into cells and through intracellular compartments. We designed the delivery system of TheraPlas™ by chemically modifying the low molecular weight polymer to improve its gene transfer activity without increasing toxicity. We believe that TheraPlas™ is a viable alternative to current approaches to gene delivery due to several distinguishing characteristics, including enhanced molecular versatility that allows for complex modifications to improve activity and safety.

TheraSilence™ Technology Platform

TheraSilence™ is a technology platform for the delivery of synthetically-generated inhibitory RNA (“RNAi”), such as small inhibitory RNAs (“siRNAs”), microRNAs, anti- microRNA mimics, microRNA mimics, and related molecules that can regulate protein expression at the transcript level by exploiting endogenous cell mechanisms. Inhibitory RNA-based therapies have the potential for targeting the disease-related genes with a high degree of specificity, including the target genes that have been widely identified as “non-druggable.” The TheraSilence™ technology seeks to address the primary obstacle to nucleic acid-based therapeutics, which is the efficient delivery of RNAs to target cells. Specifically, a delivery system needs to be able to protect the RNAi from nuclease degradation, transfer the molecule across the cellular membranes and release the material so that it can be available to the endogenous RNA silencing machinery. We have developed proprietary, novel structures that we believe are able to interact with the RNAi molecules forming protective nanoparticles that can be readily taken up into cells. In addition, these systems are chemically flexible and amenable to attachment of tissue-targeted ligands, in-vivo stabilizing agents and other functional moieties which can tailor a formulation for a particular application and delivery modality. We believe that these features can provide high specificity for RNAi delivery to select tissue, enhance stability and reduce in-vivo toxicity. In-vivo proof-of-concept studies of our most advanced system have shown the ability to deliver RNAi molecules specifically to the pulmonary vascular following intravenous administration. Using this delivery system we have been able to show in mice that delivery of a siRNA molecule that targets anti-vascular endothelial receptor 2 (“VEGF2”), a protein that is critical for the growth of new blood vessels in tumors, can significantly inhibit lung tumor growth. Additionally, delivery of an anti-micro RNA molecule into rats with experimentally induced pulmonary arterial hypertension was able to normalize vascular remodeling that occurs in the lung and restore cardiac function that is compromised as a result of the disease. This suggests that this delivery system can effectively deliver numerous potentially therapeutic molecular targets and may have application for the treatment of numerous lung diseases.

Technology Development and Licensing Agreements

On August 9, 2016, we signed a long-term Technology Transfer, Manufacturing and Commercial Supply Agreement (the “GEN-1 Agreement”) with Hisun to pursue an expanded partnership for the technology transfer relating to the clinical and commercial manufacture and supply of GEN-1, Celsion’s proprietary gene mediated, IL-12 immunotherapy, for the greater China territory, with the option to expand into other countries in the rest of the world after all necessary regulatory approvals are in effect. The GEN-1 Agreement will help to support supply for both ongoing and planned clinical studies in the United States, and for potential future studies of GEN-1 in China. GEN-1 is currently being evaluated by Celsion in first line ovarian cancer patients.