



INITIATION OF COVERAGE

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IMMUNOCELLULAR THERAPEUTICS LTD. (OTCBB: IMUC)

ImmunoCellular – A Specialist in Targeting Cancer Stem Cells

ImmunoCellular Therapeutics is a development stage company dedicated to immunological therapies targeting cancer stem cells. Its two technology platforms have created “active” and “passive” immunotherapies against a wide range of cancers. The most advanced candidate is the ICT-121 vaccine, which uses a validated cancer stem cell molecule, CD133, to arm a patient’s immune system. Preclinical research has set a firm basis for ICT-121’s clinical development, initially targeting the most common and deadliest brain cancer, glioblastoma.

The Company’s “passive” immunotherapy program, based on DIAAD technology, has generated monoclonal antibodies against

Share Price (04/03/09)	\$0.37
52-Week Price Low / High	\$0.15 - \$0.70
Mkt. Capitalization (issued)	\$4.69 M
Shares Outstanding (issued)	12.68 M
12-month Target Price	\$2.50
Website	www.imuc.com

specific cancer cell antigens. One project has created a potential therapy for pancreatic and small cell lung cancers, while another has yielded antibodies that recognize multiple myeloma and ovarian cancer.

We note that the immunotherapy programs are in sync with personalized medicine in that they may yield both effective immunotherapies and diagnostic tests to ensure optimal use.

We are initiating coverage on ImmunoCellular Therapeutics Ltd. (OTCBB: IMUC) with a Buy rating and a 12-month price target of \$2.50 for IMUC shares.

KEY INVESTMENT POINTS:

- **TWO PLATFORMS UNDERPIN IMMUNOCELLULAR’S ASSAULT ON CANCER STEM CELLS.** The Company is applying its expertise in immunology to target the malignant stem cells that comprise a small fraction of a tumor’s cell population, but are responsible for its growth and the formation of metastases.
 - **ACTIVE IMMUNIZATION:** The Company has developed an anticancer vaccine against a proprietary glycoprotein, CD133, that is expressed in abundance by stem cells of a variety of malignancies, but not by normal adult cells. The vaccine, called ICT-121, teaches the patient’s immune system (specifically, via the formation of cytotoxic T cells) to recognize and destroy cancer stem cells. An IND is scheduled to be filed for this program in the third quarter, and initiation of a Phase I/II study is anticipated in the fourth quarter. We note, too, that the Company has developed a related vaccine, ICT-107, which employs dendritic cells, exposed to six patient-specific antigens *ex vivo*, as an inoculant.
 - **PASSIVE IMMUNIZATION:** Two programs that employ monoclonal antibodies to destroy cancer cells are approaching clinical trials. One program involves antibodies against CEACAM5 and CEACAM6, which are cell adhesion molecules that play a role in tumorigenesis and cancer

cell proliferation and migration. Preclinical work has found that the ICT-109 antibodies recognize 100% of small cell lung cancer cells and 90% of the cells comprising pancreatic tumors. A diagnostic test is being readied via a collaboration with George Mason University pursuant to initiating a clinical trial later this year. The other program involves an antigen that is highly localized to malignant cells associated with multiple myeloma and ovarian cancer. Clinical development of ICT-69 is about two years away.

- **IMMUNOCELLULAR'S R&D STRATEGY SHOULD RESONATE WITH INVESTORS.** All too often, anticancer therapies are evaluated in patients with advanced stages of a disease or with compromised immune systems, after they've undergone multiple treatment regimens over several years. These attributes have contributed to insignificant increases in patients' survival in response to immunotherapies historically. As a result, ImmunoCellular is taking a different approach by targeting cancers that are often lethal within months of being diagnosed, notably glioblastoma, multiple myeloma, and pancreatic and small cell lung cancers. This should enable its therapeutic candidates to be evaluated in patients at an earlier stage of disease progression and with a more robust immune system. Furthermore, the Company's vaccines are designed to eliminate cancer stem cells in conjunction with traditional methods of reducing a tumor's size. We believe ImmunoCellular's strategy minimizes its R&D expenses and investment risk by determining quickly the efficacy of its immunotherapies in patients who are most apt to benefit.
- **THE DIAAD PLATFORM MAY BE APPLIED TO NUMEROUS MALIGNANCIES.** This technology uses a unique approach to generating disease-specific antibodies in that it involves a process called subtractive immunization, in which an animal is first exposed to antigens associated with normal cells to induce immunological tolerance. Subsequently, exposure to cancer-related antigens *in situ* (e.g., in whole malignant cells) causes the immune system to develop a humoral or B-cell response only to antigens expressed by abnormal human cells, even if they are weak antigens. This approach yields a stronger response and one that is more effective at recognizing only exposed portions of antigens on the surface of malignant cells. (Because many other companies first isolate specific antigens for immunization, they often generate antibodies against sequestered portions of the molecules.) ImmunoCellular's initial programs utilizing the DIAAD (Differential Immunization for Antigen and Antibody Discovery) platform have successfully yielded antibodies targeting, in one case, broadly expressed cancer cell antigens and, in the other, an antigen with a far more limited expression pattern. We expect this unique technology will be employed to create an even more extensive array of antibodies targeting the very basic elements of the most dreaded malignancies.
- **ADDITIONAL VALUATION DRIVERS**
 - **IMMUNOCELLULAR IS GUIDED BY AN IMPRESSIVE TEAM** with considerable experience in the pharmaceutical industry, immunological therapy development, and oncology. Among the notable executives and advisory personnel are: **CEO Manish Singh, Ph.D.** who has served 14 years in various capacities in the drug industry and has considerable experience investing in emerging pharmaceutical companies; **Chairman & Chief Science Officer John S. Yu, M.D.**, an internationally renowned neurosurgeon and pioneer in the identification of cancer stem cells in glioblastoma tumors; and **Keith L. Black, M.D. Chairman of the Scientific Advisory Board**, who has conducted extensive research into the blood brain barrier and the development of vaccines against brain tumors.

April 27, 2009

- **CEDARS-SINAI MEDICAL CENTER SUPPORTS R&D PROGRAMS.** This internationally recognized medical center is the home of ImmunoCellular's research base and the site where Dr. John Yu conducted clinical trials of early immunotherapies against glioblastoma. It will also serve as a location for the Phase I/II trial of ICT-121 that is scheduled to start later this year.
- **IMMUNOCELLULAR HAS SECURED INTELLECTUAL PROPERTY AROUND ITS KEY PROGRAMS.** Exclusive licensing agreements to patents owned by Cedars-Sinai Medical Center have garnered protection for the cancer vaccine program. In addition, the acquisition of the DIAAD technology and related assets in 2008 secured 20 patents (issued and filed) related to monoclonal antibodies against various cancers, including myeloma, pancreatic, and small cell lung cancers.
- **VALUATION: IMUC SHARES ARE GREATLY UNDERVALUED.** We believe ImmunoCellular has a unique set of therapies to offer oncologists in their fight against their unrelenting nemesis, cancer stem cells. Moreover, the two innovative technology platforms offer the opportunity to create similar immunotherapies for virtually any malignancy, and the Company has a team of executives capable of bringing the corporate plans to fruition. Given the characteristics of its passive immunotherapies, we expect the Company will successfully partner at least one of its antibodies this year. A review of recent transactions suggests that the deal will generate \$20 million to \$30 million for ImmunoCellular, which will be used to finance the clinical development of ICT-121. (The Company currently has ample cash to finance operations through mid-2010.) Achievement of this milestone and progress with ICT-121's development should drive the valuation of IMUC shares in the near term. Further out, data from the ICT-121 clinical program may well have the effect that good news on the immunotherapy Provenge had on **Dendreon's (NasdaqGM: DNDN)** share price – more than doubling the valuation overnight. Our discounted cash flow model and a transactions analysis value IMUC shares at \$2.50 and \$3.10 each, respectively. Accordingly, we are initiating a BUY recommendation on ImmunoCellular Therapeutics and establishing a 12-month target price of \$2.50 per share.

*Mark Merrill at Griffin Securities, Inc. assisted with the research of this report.



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CORPORATE ACHIEVEMENTS

Nov '06	Acquired worldwide license from Cedars-Sinai Medical Center for cell therapies, including dendritic cell (DC) vaccines for neurological disorders.
Nov '06	Changed corporate name from Spectral Molecular Imaging to ImmunoCellular Therapeutics, Ltd. to reflect the new focus of the Company.
May '07	Initiated Phase I clinical trial of ICT-107, a dendritic cell vaccine created with glioblastoma tumor lysate antigens.
Nov '07	Filed two patent applications covering its multiple-antigen DC vaccine for cancer and cancer stem cell vaccine technologies.
Feb '08	Acquired DIAAD technology from Molecular Discoveries that enables the rapid discovery of antibodies that diagnose and treat cancers, along with certain antibodies recognizing multiple myeloma, colon, small cell lung, pancreatic and ovarian cancers.
May '08	Completed proof-of-principle research of vaccine based on a single protein.
June '08	Entered into collaboration with George Mason University for the development of antibody-based diagnostic assays to detect small cell lung and pancreatic cancers.
July '08	Licensed technology from Cedars-Sinai Medical Center for peptides for a dendritic cell vaccine capable of eliciting a T cell response to cancer stem cells.
Oct '08	Granted two patents on lead antibody drug candidate, ICT-109, which is being developed for small cell lung and pancreatic cancers.
Dec, '08	Reported positive preliminary data from ICT-107 Phase I clinical trial, in which 50% of the patients had a tumor-specific immune response.

UPCOMING MILESTONES

Q2, 2009	Present ICT-107 immunological data and clinical results at ASCO meeting.
Q3, 2009	File ICT-121 IND with the FDA.
Q3, 2009	Complete preliminary feasibility data on the use of ICT-109 as a diagnostic tool for lung and pancreatic cancers.
Q4, 2009	Enter into a pharma/biotech partnering deal involving one of the monoclonal antibodies programs.
Q4, 2009	Initiate patient enrollment in ICT-121 Phase I/II clinical trial.
Q1, 2010	Enter into a partnering deal for ICT-107.
Q2, 2010	Evaluate preliminary immune response data from patients treated with ICT-121.
Q3, 2010	Enter into a pharma/biotech deal on a second antibody program.
Q4, 2010	Present complete immune response and survival data on ICT-121 at SNO meeting.



MANAGEMENT TEAM

Manish Singh, Ph.D., M.B.A.: President, CEO, & Board of Directors member

- Served as Director of California Technology Ventures, where he was co-lead in investments in multiple biotechnology companies, including Aliva Biopharmaceuticals, SurgRx, and Ceregene.
- Has 14 years of pharmaceutical industry experience in research, product development, manufacturing, and business development.
- Holds ten issued patents and patent applications.

John S. Yu, M.D.: Chief Science Officer & Chairman of the Board

- An internationally renowned neurosurgeon on the faculty of Cedars-Sinai Medical Center.
- Research scientist focused on immune and gene therapies for brain tumors.
- Recipient of numerous awards, including the Preuss Award (American Association of Neurological Surgeons and Congress of Neurologic Surgeons) and the Academy Award (American Academy of Neurological Surgery).

C. Kirk Peacock: CFO

- A Certified Public Accountant with experience as the Chief Financial Officer of both public and private companies, including CytRx, DigitalMed, and Ants.Com.
- Director and audit committee member of Laird Norton Company.

James G. Bender, Ph.D., M.P.H.: VP, Clinical Development

- Has more than 20 years of clinical development experience that includes work with a cancer vaccine at IDM Pharma and with stem cell and cancer vaccine products at Nexell Therapeutics.
- Has more than 75 scientific publications and is listed as an inventor on 11 patents.

BOARD OF DIRECTORS

Jacqueline Brandwynne

- President & CEO of Brandwynne Corporation, which has co-founded and assisted in the development of several healthcare and biotech companies.
- Business strategist with more than 25 years of experience working with consumer products, pharmaceutical/chemical, and financial service companies.

Colonel Richard A. Cowell

- Principal at Booz Allen Hamilton, Inc., where he is involved in advanced concepts, technology experimentation and integration, and establishing new business operations.
- Director and chair of the audit committee of Microvision.



Navdeep Jaikaria, Ph.D.

- Former managing director of equity research and senior biotechnology analyst at Rodman & Renshaw.
- Consultant to pharmaceutical and biotechnology companies.

Robert L. Martuza, M.D.

- Chief of Neurosurgery Service at Massachusetts General Hospital and Higgins Professor of Neurosurgery at Harvard Medical School.
- Recognized authority on neurosurgery with numerous published articles and books and 11 patents issued or pending on cell therapy.

SCIENTIFIC ADVISORY BOARD

Keith L. Black, M.D.: Chairman, Scientific Advisory Board

- Chairman of the Department of Neurosurgery and Director of the Maxine Dunitz Neurosurgical Institute at Cedars-Sinai Medical Center.
- Member of the editorial boards of *Neurological Research*, *Gene Therapy* and *Molecular Biology, Neurosurgery Quarterly* and *Frontiers In Bioscience*.
- Research scientist with extensive publications on opening the blood brain barrier to chemotherapeutic agents and on developing vaccines against brain tumors.

Peter Brooks, Ph.D.

- Research scientist focused on studying mechanisms that regulate angiogenesis, tumor growth and metastasis.
- Co-founder of Cell Matrix, a corporation with anti-angiogenic drugs, including a humanized monoclonal antibody, for treating malignant tumors.

Silvia Chiara Formenti, M.D.

- Chairman of the Department of Radiation Oncology at New York University, with considerable experience in breast and cervical cancer research.
- Pioneer in the concurrent use of chemo-radiation prior to surgery.

Sherie Morrison, Ph.D.

- Professor of Microbiology, Immunology and Molecular Genetics at the University of California, Los Angeles.
- Research scientist focused on the functional properties of antibodies and antibody-related proteins.

THE “ACTIVE” IMMUNOTHERAPY PLATFORM

Active immunotherapy involves eliciting a direct response from a patient’s own immune system in the form of antibody production or T cell lymphocyte activation. This is quite distinct from passive immunity in which antibodies against a specific antigen(s) are administered in lieu of stimulating the patient’s own immune system. Each of these approaches has a place in physicians’ armamentarium against disease, and ImmunoCellular Therapeutics is employing both to create highly specific oncological medicines.

CANCER STEM CELLS & CD133

Only a fraction of the cells comprising a tumor are capable of tumor generation upon transplantation, and identifying these cancer stem cells has been a challenge. The first breakthrough came in a study of a hematological malignancy,¹ which was followed several years later by a discovery that glioblastoma tumors contain a small number of cells capable of giving rise to all cell types found in such neoplasms.² The stem cell theory of cancer attributes the formation, growth, and metastasis of malignancies to these cells. The problem confronting medical science today is how to target this relatively small population of cells that generally possess strong survival skills against radiation and pharmaceutical intervention.

ImmunoCellular has succeeded in developing a vaccine targeting cancer stem cells via a proprietary antigen expressed specifically by stem cells of numerous types of cancer. CD133 is an 865 amino acid glycoprotein that traverses the cell wall, with a sizable proportion of the molecule exposed to the extracellular milieu. This molecule is a member of a family of compounds, whose structures have been partially conserved through evolution. (For instance, human and mouse CD133 molecules have 60% homologous amino acid sequences.) The physiological function of CD133, which is also known as prominin-1, is not fully understood. It appears to organize the lipid topology of the cell membrane, thereby helping to sustain the stem cell phenotype (i.e., prevent differentiation). As such, the glycoprotein is expressed at low levels on progenitor cells in normal adult tissues, including brain, gut, kidney, pancreas, and skin.³

Malignant cells are a different matter. The stem cell theory of cancer postulates that neoplastic cells are derived from stem cells or their daughters, progenitor cells that are capable of self-replication and of differentiating into a limited number of cell types. They should be found in relatively small numbers in a tumor, but act as an important source of growth. According to the stem cell theory of cancer, cells exhibiting CD133 should be found in many, if not all tumors, and that is exactly what has been observed experimentally – CD133 has been found in brain, prostate, pancreatic, colon, primary liver, thyroid, and kidney cancers.^{3,4} Moreover, CD133⁺ cells comprise a fraction of the total cells in a tumor and are capable of differentiating in culture into malignant cells resembling those in the original tumor.²

An important consequence of the stem cell theory is that any attempt to eradicate a malignancy will ultimately fail unless it eliminates the cancer stem cells. This is consistent with clinical results, as a hallmark of the deadliest tumors is their ability to regenerate. ImmunoCellular and other investigators

¹ Lapidot, T, et al. A cell initiating human acute myeloid leukemia after transplantation into SCID mice. *Nature* (1994); 367: 645.

² Singh, SK, et al. Identification of a cancer stem cell in human brain tumors. *Cancer Res* (2003); 63: 5821.

³ Mizrak, D, et al. CD 133: molecule of the moment. *J Pathol* (2008); 214: 3.

⁴ Zito, G, et al. *In vitro* identification and characterization of CD133^{pos} cancer stem-like cells in anaplastic thyroid carcinoma cell lines. *PLoS ONE* (2008); 3(10): e3544.

have examined the properties of CD133⁺ cells and found some disconcerting traits. For instance, radiation and chemotherapy result in a higher prevalence of CD133⁺ cells in the regenerated tumor than in the primary tumor.^{5,6,7} In other words, today's therapies preferentially allow the most proliferative cells within a malignancy to survive. Research into the underlying causes of this phenomenon has found that the cells often rely on multiple mechanisms to protect themselves against such insults as anticancer treatments. Notably, CD133⁺ cells overexpress genes that are related to drug resistance and are involved in inhibiting cell apoptosis. Among these are the drug transporter BCRP1; the DNA repair protein MGMT, which protects against the effects of such alkylating agents as temozolomide; the anti-apoptotic genes FLIP, BCL-2, and BCL-XL; members of the inhibitors of apoptosis protein family; and SIRT1, which acts to sequester the pro-apoptotic factor BAX away from mitochondria. These cells also have the ability to activate a DNA checkpoint pathway that is normally used during replication to protect against mismatched base pairs, but that can be used by cancer cells to repair radiation-induced chromosomal damage.

Another trait that contributes to the aggressiveness of tumors expressing CD133 is the protein's association with cells having a greater migratory index.⁸ This characteristic cannot yet be attributed specifically to the CD133 protein, but it is a trait of CD133⁺ cells. Indeed, the greater migratory index may reflect any of the other genes expressed differently between CD133⁻ and CD133⁺ cells.

ICT-121: IMMUNOCELLULAR'S LEAD VACCINE

ICT-121 consists of a nine amino acid epitope of CD133, combined with the immune stimulant GM-CSF (granulocyte macrophage-colony stimulating factor) as an adjuvant. Initially, it will be tested as a therapy for glioblastoma, though it may prove effective against a wide range of cancers. ImmunoCellular has several patents covering different aspects of this vaccine,⁹ and it recently hired a formulation specialist to prepare a stable form of the antigen to avoid the need to store it frozen. This work should be completed within a few months, and preparations are under way to render the vaccine useful for patients regardless of their HLA-A phenotypes. (The human leukocyte antigen, or HLA, system is the major histocompatibility complex in humans that presents unrecognized antigens to the immune system.) The current version of ICT-121 is useful for only patients in the HLA-A2 group. But thanks to a recent development garnering additional HLA proteins, the vaccine will be suitable for all patients.

The Company intends to develop ICT-121 initially for two deadly cancers. The first clinical study will build upon ImmunoCellular's experience in glioma and glioblastoma. As described in the box below, this is an insidious disease for which there are few options. Accordingly, even a moderate improvement in the time to disease progression and survival might well result in ICT-121 becoming the first therapy approved specifically for targeting cancer stem cells. The second clinical development path will probably test the vaccine against pancreatic cancer, which is also discussed separately below. As with glioblastoma, the

⁵ Liu, G, et al. Analysis of gene expression and chemoresistance of CD133⁺ cancer stem cells in glioblastoma. *Mol Cancer* (2006); 5: 67.

⁶ Bao, S, et al. Glioma stem cells promote radioresistance by preferential activation of the DNA damage response. *Nature* (2006); 444: 756.

⁷ Blazek, ER, et al. Daoy meduloblastoma cells that express CD133 are radioresistant relative to CD133⁻ cells, and the CD133⁺ sector is enlarged by hypoxia. *Int J Radiation Oncol Biol Phys* (2007); 67(1): 1.

⁸ Beier, D, et al. CD133⁺ and CD133⁻ glioblastoma-derived stem cells show differential growth characteristics and molecular profiles. *Cancer Res* (2007); 67(9): 4010.

⁹ Four patents related to this active immunotherapy program have been filed, and additional applications are in process.



average pancreatic cancer patient's survival is measured in months. And like glioblastoma, pancreatic cancer stem cells express CD133 at unusually high levels.

Glioblastoma multiforme is the most common and deadliest of brain tumors. The latest data on malignancies of the central nervous system found that 75% of all primary brain and CNS tumors reported in the United States were gliomas, of which 51% were glioblastomas.¹⁰ The standard of care consists of surgery and radiation therapy to debulk the tumor and provide local control, and temozolomide (sold as Temodar[®] by **Schering-Plough [NYSE: SGP]**) to cytereduce any remaining tumor and eradicate micrometastatic disease. Another drug, carmustine (sold in an implantable wafer as Gliadel by **Esai's** MGI Pharma subsidiary), is also used to combat brain tumors. Yet, only 27% of glioblastoma patients survive for 24 months.¹¹ The American Cancer Society estimates that more than 13,000 patients in the United States will succumb to brain malignancies this year.¹²

The clinical development program of ICT-121 is scheduled to begin later this year. ImmunoCellular intends to file an IND with the FDA in the third quarter, which should enable ICT-121 to enter a clinical trial before the year ends. The Phase I/II study will evaluate the vaccine's safety in 18-20 patients with glioma or glioblastoma. The trial protocol, which has yet to be finalized, calls for different ICT-121 regimens for newly diagnosed patients and those with recurrent disease. (Newly diagnosed patients will receive ICT-121 in conjunction with the standard of care in the Phase II portion of the trial, while recurrent disease will be treated with ICT-121 alone in both phases of the trial.) Each patient's immune response to CD133 will be evaluated before and after the vaccine therapy in peripheral blood mononuclear cells by monitoring γ -interferon production. In a previous clinical trial, the Company has found that results of this test are strongly correlated with clinical responses (see Figure 1 on the next page).¹³ Clinical efficacy will be assessed based on disease-free survival. The trial will be conducted at Cedars-Sinai Medical Center and other hospitals with oncology programs, which should facilitate patient selection and physician involvement. We believe the trial will be completed in late 2010. A subsequent Phase II/III trial may be sufficient to gain regulatory approval for commercialization. The same endpoints probably will be used with enough patients to detect significance in a three-month increase in disease-free survival. We believe the pancreatic cancer study will commence about two years after the glioblastoma trial begins.

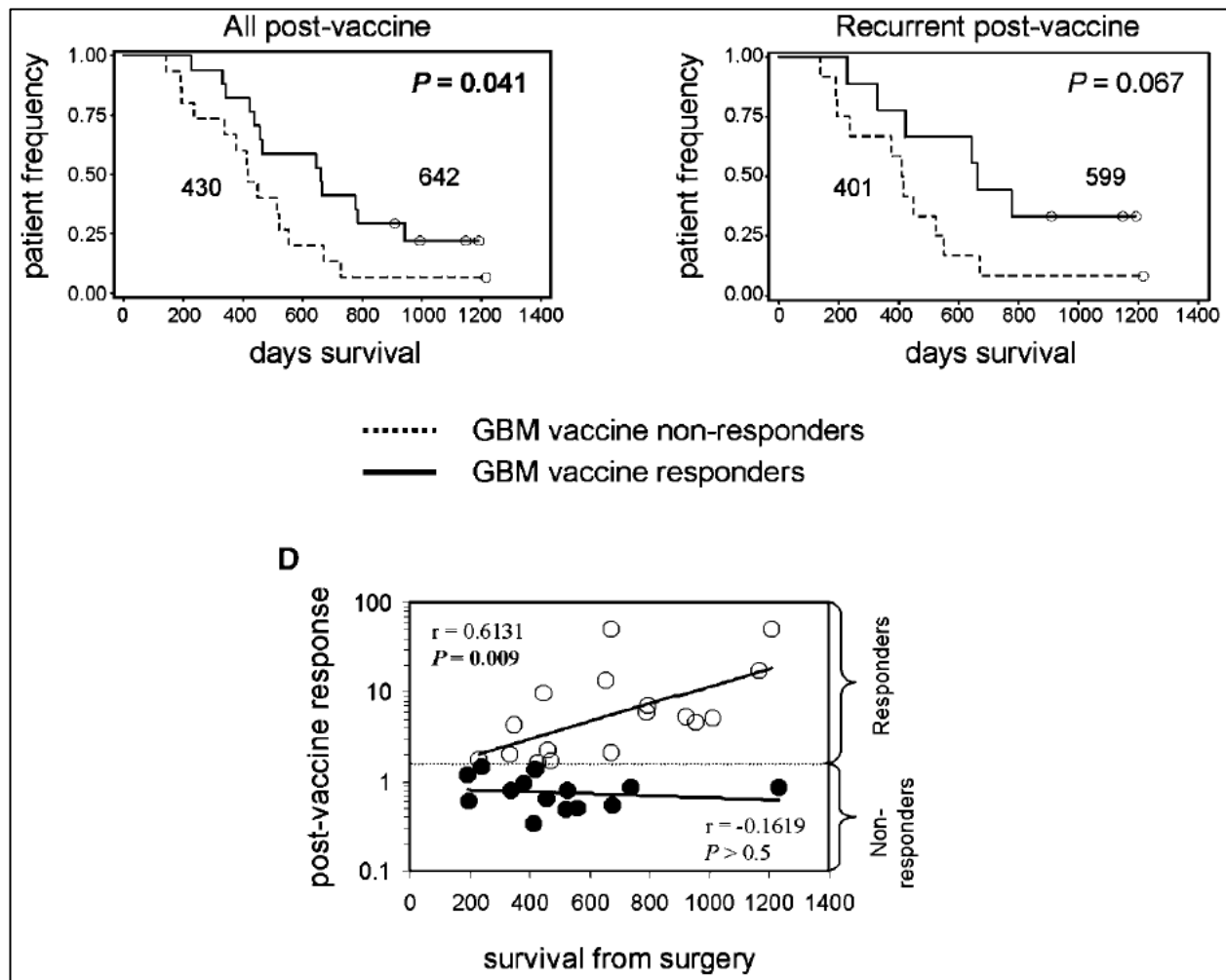
¹⁰ CBTRUS. 2007-2008 Primary Brain Tumors in the United States.

¹¹ Stupp, R, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomized phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol* (2009); March 6 epub.

¹² Cancer Facts & Figures 2008, published by the American Cancer Society.

¹³ Wheeler, CJ, et al. Vaccination elicits correlated immune and clinical responses in glioblastoma multiforme patients. *Cancer Res* (2005); 68(14): 5955.

Figure 1. Correlation between immune and clinical responses in glioblastoma patients.



Source: Wheeler, CJ, et al.¹³

Figure 1. Patients with glioblastoma were treated with a dendritic cell vaccine, similar to ICT-107 (discussed on page 13), but based on glioblastoma lysate rather than the specific proteins used in preparing ICT-107. Cytokine responsiveness, assessed as γ -interferon production, was measured in the peripheral blood of 32 patients prior to and after administration of the vaccine. Patients who failed to demonstrate an increase in antigen-directed γ -interferon production had shorter post-surgery survival times, regardless of whether their disease was recurrent or newly diagnosed.

Pancreatic cancer is a disease that is rarely diagnosed at an early stage. Indeed, only 10%-20% of newly diagnosed patients are considered eligible for surgical resection, and even then, surgical resection is far from curative.¹⁴ A decade's experience at a leading U.S. cancer center shows that Stage I and II pancreatic cancer patients who underwent surgery had a mean survival of roughly 25 months, versus about 10 months for those who did not. Overall, an estimated 37,170 patients were diagnosed last year in the United States, of whom 91% succumbed to the disease.¹² The statistics are worse on a global basis, for an estimated 232,000 people were diagnosed in 2002, with 227,000, or 97.8%, dying of the disease that same year.¹⁵ Attempts to improve survival of resected patients via adjunctive chemotherapy have yielded no improvements since 1985, and all standard treatments involving combinations of radiation and chemotherapeutic agents (including the anti-angiogenesis drug bevacizumab, sold as Avastin by **Genentech [NYSE: DNA]**) have limitations, as the disease is extremely resistant to both types of intervention.

ICT-121 is designed to complement the current standard of care for glioblastoma and pancreatic cancer. This approach makes sense from both clinical and commercial standpoints.¹⁶ Surgical removal of the tumor is important simply for reducing the malignant mass, thereby giving the immune system a smaller and more manageable target to destroy. Radiation therapy should provide a similar benefit, while perhaps also altering the microenvironment of the tumor to increase the number of infiltrating lymphocytes. Combining the vaccine with chemotherapy has the potential to generate synergistic effects. Research has found that some chemotherapies, such as 5-fluorouracil, 5-aza-2-deoxycytidine, melphalan, and mitomycin C, increase the expression of some tumor antigens, while paclitaxel induces cytokine production that promotes T-cell cytotoxicity. Even use of a metronomic dosing regimen for chemotherapy can prove helpful by facilitating passage of T cells through the tumor vasculature. Thus, there are valid clinical reasons to add a vaccine to the standard of care. There is also a commercial reason – ImmunoCellular's vaccine will not pose a competitive threat to surgeons, radiologists, or manufacturers of chemotherapeutic medicines. As a result, it probably will be adopted more readily than if it were intended to replace any of the standard treatments in use.

¹⁴ Katz, MHG, et al. Tumor-node-metastasis staging of pancreatic adenocarcinoma. *CA Cancer J Clin* (2008); 58(2): 111.

¹⁵ DeVita, VT, TS Lawrence, SA Rosenberg. *Cancer: Principles & Practice of Oncology*. Philadelphia: Lippincott, Williams & Wilkins, 2008.

¹⁶ Emens, LA and Jaffee, EM. Leveraging the activity of tumor vaccines with cytotoxic chemotherapy. *Cancer Res* (2005); 65(18): 8059.

ICT-107: A DENDRITIC CELL VACCINE

Dendritic cells (DCs) play a central role in the immune system by processing antigens for presentation to effector cells (i.e., helper and cytotoxic T lymphocytes, natural killer T and B cells). A number of attempts have been made to exploit the unique capabilities of DCs to stimulate the immune system to recognize various cancers. This has entailed exposing DCs *ex vivo* to either antigen mixtures prepared from a patient's tumor or specific antigens known to be expressed by malignant cells. Early attempts were met with mixed results, characterized by good safety profiles but generally weak immune responses. Optimization work has helped generate DC vaccines against the following neoplasms: gastric,¹⁷ ovarian,¹⁸ prostate,¹⁹ breast,²⁰ pancreatic,²¹ biliary,⁶ lung,²² and colorectal²³ cancers, as well as glioblastoma,^{24,25} renal cell carcinoma,²⁶ leukemia,¹ and melanoma.²⁷ Adverse events reported thus far have been mild to moderate in nature, in stark contrast to the toxicities associated with chemotherapeutic agents. Nonetheless, dendritic cell vaccines have not been approved by the major regulatory agencies worldwide, though that may soon change following the successful clinical trial of Dendreon Corporation's Provenge vaccine against prostate cancer.

ImmunoCellular has focused its DC vaccine program on neurological disorders, including malignancies and neurodegenerative diseases. The initial vaccine, ICT-107, is a patient-specific therapeutic agent, created by exposing DCs to six antigens isolated from a patient's malignant brain tissue after surgery. The vaccine has successfully completed a Phase I clinical trial at Cedars-Sinai Medical Center, where it was developed. Preliminary results from the 19-patient study revealed no serious side effects and provided encouraging efficacy data, as 50% of the patients exhibited a tumor-specific immune response and 42% survived for at least a year after undergoing surgical resection.²⁸ Fully analyzed data from the ICT-107 trial is scheduled for presentation at the American Society of Clinical Oncology (ASCO) meeting, which will be held from May 29th through June 2nd. Rather than develop this therapy further, the Company intends to seek a partner to take the project forward.

¹⁷ Li, YL, et al. Bone marrow derived dendritic cells pulsed with tumor lysates induce anti-tumor immunity against gastric cancer *ex vivo*. *World J Gastroenterol* (2008); 14(46): 7127.

¹⁸ Hernando, JJ, et al. Vaccination with dendritic cells transfected with mRNA-encoded folate-receptor-alpha for relapsed metastatic ovarian cancer. *Lancet Oncol* (2007); 8(5): 451.

¹⁹ Lehrfeld, TJ, and Lee, DI. Dendritic cell vaccines for the treatment of prostate cancer. *Urol Oncol* (2008); 26(6): 570.

²⁰ Czerniecki, BJ, et al. Development of vaccines for high-risk ductal carcinoma in situ of the breast. *Cancer Res* (2007); 67(14): 6531.

²¹ Lepisto, AJ, et al. A phase I/II study of a MUC1 peptide pulsed autologous dendritic cell vaccine as adjuvant in patients with resected pancreatic and biliary tumors. *Cancer Ther* (2008); 6(B): 955.

²² Zhong, H, et al. Low-dose paclitaxel prior to intratumoral dendritic cell vaccine modulates intratumoral cytokine network and lung cancer growth. *Clin Cancer Res* (2007); 13(18): 5455.

²³ Liu, KJ, et al. Generation of carcinoembryonic antigen (CEA)-specific T-cell responses in HLA-A0201 and HLA-A2402 late-stage colorectal cancer patients after vaccination with dendritic cells loaded with CEA peptides. *Clin Cancer Res* (2007); 10: 2645.

²⁴ Yu, JS, et al. Vaccination with tumor lysate-pulsed dendritic cells elicits antigen-specific cytotoxic T-cells in patients with malignant glioma. *Cancer Res* (2004); 64: 4973.

²⁵ De Vleeschouwer, S, et al. Postoperative adjuvant dendritic cell-based immunotherapy in patients with relapsed glioblastoma multiforme. *Clin Cancer Res* (2008); 14(10): 3098.

²⁶ Uemura, H, and De Velasco, MA. Tumor vaccines in renal cell carcinoma. *World J Urol* (2008); 26(2): 147.

²⁷ Lopez, MN, et al. Prolonged survival of dendritic cell-vaccinated melanoma patients correlates with tumor-specific delayed type IV hypersensitivity response and reduction of tumor growth factor beta-expressing T cells. *J Clin Oncol* (2009); 27(6): 945.

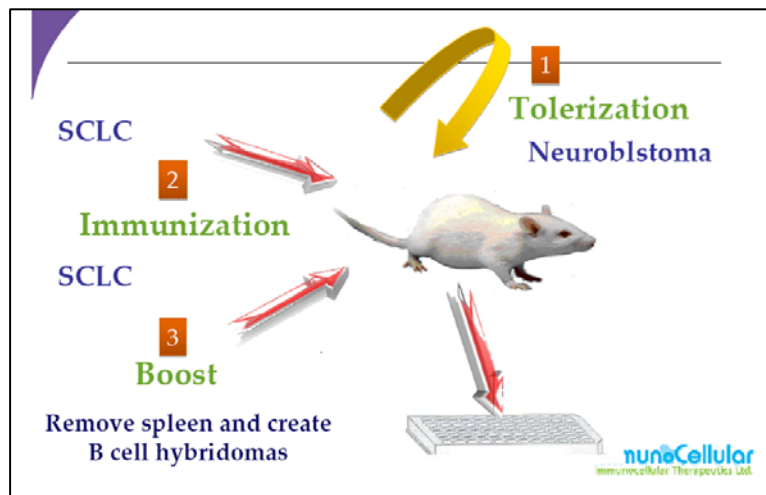
²⁸ ImmunoCellular Therapeutics press release, dated December 23, 2008.

IMMUNOCELLULAR’S “PASSIVE” IMMUNOTHERAPY PROGRAM

In February 2008, the Company acquired from Molecular Diagnostics a platform technology, dubbed DIAAD, for the rapid discovery of antibodies to diagnose and combat cancer and chronic diseases. The deal also garnered monoclonal antibodies with the potential to detect and treat multiple myeloma, small cell lung, pancreatic, and ovarian cancers.

As illustrated in Figure 2, DIAAD uses immunological tolerance to expedite the identification of molecular differences between normal and disease-related cells and to produce monoclonal antibodies against disease-specific antigens. (Development of tolerance is a normal mechanism of the immune system that instructs the body’s defenses to recognize “self” and thereby avoid mounting an attack against its own tissues, resulting in an autoimmune disease.) This approach yields a stronger response against the cancer-related antigens than otherwise possible.

Figure 2. The DIAAD Protocol



Source: ImmunoCellular Therapeutics

ICT-109 & ICT-37

These drug candidates are monoclonal antibodies targeting different sites on molecules associated with a large number of cancers. Specifically, ICT-109 recognizes an epitope on two members of the carcinoembryonic antigen (CEA) family, CEACAM5 and CEACAM6, while ICT-37 targets an antigenic site found only on CEACAM5. These highly glycosylated proteins are attached via a glycoposphatidylinositol anchor (i.e., a phospholipid with sugar moieties) to the exterior of the cell membrane, where they function as cell adhesion molecules. Related glycoproteins have been implicated in forming/maintaining a tissue’s normal structural architecture and in contributing to the development of non-cancerous

pathological conditions.^{29,30,31} It's only been fairly recent that their contribution to the formation, proliferation, and migration of cancer cells has been fully appreciated.

The targets of ICT-109 and ICT-37 play a role in tumorigenesis. Research has found that CEACAM5 is overexpressed in pre-cancerous cells of the colonic mucosa, suggesting that it contributes to the eventual transformation to the malignant state.³² Likewise, the presence of CEACAM6 in atypical ductal hyperplasias (precancerous cells) has been strongly correlated with the development of invasive breast cancer.³³

Overexpression of CEACAM5 and CEACAM6 supports cell proliferation in several ways. For one, they impair differentiation, thereby favoring preservation of the cancer stem cell phenotype. In other words, they act to ensure the source of a malignant growth. This capability has been observed in various cell types, including skeletal muscle,³⁴ and colon and fat cells.³⁵ In addition, these glycoproteins impede apoptosis, which is the self-destruct pathway of normal cells.³⁶ They also protect against chemo- and radiation therapy, notably in small cell lung and pancreatic cancer cells.^{37,38} The mechanism involved does not induce multi-drug resistance. Rather, the cell adhesion molecules appear to alter the cell-matrix interaction at the tumor-stroma interface, probably via an integrin-mediated process.³⁹

CEACAM5 and CEACAM6 contribute to cancer cell migration. Normally, when a cell loses contact with its neighbors or the extracellular matrix, it self-destructs via a process called anoikis. CEACAM5 and CEACAM6 prevent anoikis, for example in pancreatic cancer cells.⁴⁰ Moreover, the presence of these molecules on a cancer cell increases its metastatic potential. In pancreatic cancer, CEACAM6 enhances the cells' invasiveness via an increased expression of matrix metalloproteinase 9 (MMP9).⁴¹ (MMP9 is one of several enzymes that are used to break down the extracellular matrix for such normal physiological purposes as tissue remodeling and embryonic development and during various disease states, including

²⁹ Krauss, RS, et al. Close encounters: regulation of vertebrate skeletal myogenesis by cell-cell contact. *J Cell Sci* (2005); 118(Pt 11); 2355.

³⁰ Katidou, M, et al. The immunoglobulin superfamily of neuronal cell adhesion molecules: lessons from animal models and correlation with human disease. *Biotechnol J* (2008); 3: 1564.

³¹ Gonzales-Amaro, R, et al. Adhesion molecules in inflammatory diseases. *Drugs* (1998); 56(6): 977.

³² Ilantzis, C, et al. Cell-surface levels of human carcinoembryonic antigen are inversely correlated with colonocyte differentiation in colon carcinogenesis. *Lab Invest* (1997); 76: 703.

³³ Poola, I, et al. Expression of carcinoembryonic antigen cell adhesion molecule 6 oncoprotein in atypical ductal hyperplastic tissues is associated with the development of invasive breast cancer. *Clin Cancer Res* (2006); 12(15): 4773.

³⁴ Eidelman, FJ, et al. Human carcinoembryonic antigen, an intercellular adhesion molecule, blocks fusion and differentiation of rat myoblasts. *J Cell Biol* (1993); 123: 467.

³⁵ Ilantzis, C, et al. Deregulated expression of the human tumor marker CEA and CEA family member CEACAM6 disrupts tissue architecture and blocks colonocyte differentiation. *Neoplasia* (2002); 4(2): 151.

³⁶ Soeth, E, et al. Controlled ribozyme targeting demonstrates an antiapoptotic effect of carcinoembryonic antigen in HT29 colon cancer cells. *Clin Cancer Res* (2001); 7(7): 2022

³⁷ Kraus, AC, et al. *In vitro* chemo- and radio-resistance in small cell lung cancer correlates with cell adhesion and constitutive activation of AKT and MAP kinase pathways. *Oncogene* (2002); 21: 8683.

³⁸ Duxbury, MS, et al. A novel role for carcinoembryonic antigen-related cell adhesion molecule 6 as a determinant of gemcitabine chemoresistance in pancreatic adenocarcinomas cells. *Cancer Res* (2004); 64(11): 3987.

³⁹ Hazlehurst, LA, et al. Adhesion to fibronectin via beta1 integrins regulates p27kip1 levels and contributes to cell adhesion mediated drug resistance (CAM-DR). *Oncogene* (2000); 19(38): 4319.

⁴⁰ Duxbury, MS, et al. CEACAM6 gene silencing impairs anoikis resistance and in vivo metastatic ability of pancreatic adenocarcinomas cells. *Oncogene* (2004); 23: 465.

⁴¹ Duxbury, M, et al. CEACAM6 is a determinant of pancreatic adenocarcinomas cellular invasiveness. *Br J Cancer* (2004); 91: 1384.

arthritis.) An investigation involving the interaction between Kupffer cells (phagocytes in the liver) and colon cancer cells determined that cytokines secreted by Kupffer cells stimulated production of CEACAM5, resulting in an increased metastatic potential of the colon cancer cells.⁴² This probably contributes to the relatively high frequency in which colorectal cancer metastasizes to the liver. Finally, we note that CEACAM5 and CEACAM6 are co-localized with lipid rafts of the cell membrane and integrin $\alpha\beta 1$, which is an important element in normal cell migration and adhesion during embryonic development.

In sum, these properties of the cell adhesion molecules support the transition from a quasi-normal cell to a malignant state, maintain cancer stem cells by preventing differentiation, impart the neoplastic cells with an ability to survive chemotherapy and radiation, and facilitate the formation of metastases. These properties are borne out by clinical observations, for tumors expressing CEACAM5 and CEACAM6 typically have a poor prognosis.

CEACAM5 and CEACAM6 have attracted attention as targets for anticancer therapies. Indeed, preclinical research has shown that antibodies against these glycoproteins merit consideration for clinical use. An antibody against CEACAM6 inhibited the growth of thyroid cancer xenografts and sensitized them to a chemotherapeutic agent, dacarbazine,⁴³ while another approach found that doxorubicin potentiated the efficacy of a radiolabeled antibody against the adhesion molecule in this malignancy.⁴⁴ Another group studied the efficacy of an antibody drug conjugate specific for CEACAM6 against a pancreatic xenograft. Myelosuppression was dose limiting, though pretreatment with unconjugated antibody was found to prevent a radiolabeled version of the antibody from reaching the bone marrow without preventing its concentration within the tumor.⁴⁵

The few clinical trials that have been conducted with such antibodies have yielded mixed results. A Phase I trial of a radiolabeled antibody and doxorubicin drug regimen found a modest benefit in patients with an advanced medullary thyroid cancer.⁴⁶ On the other hand, radioimmunotherapy targeting CEACAM6 after salvage resection of colorectal liver metastases, which was studied in 23 patients, increased the median disease-free survival by 50%, from 12 months to 18 months. Overall survival rates from Kaplan-Meier analyses yielded an improvement associated with the therapy, with 42.1% of the patients surviving for five years, versus 15.8% of the controls.⁴⁷ Though encouraging, a confirmatory study involving a much larger patient population will be required to further assess the benefit.

⁴² Minami, S, et al. Role of carcinoembryonic antigen in the progression of colon cancer cells that express carbohydrate antigen. *Cancer Res* (2001); 61(6): 2732.

⁴³ Stein, R, and Goldenberg, DM. A humanized monoclonal antibody to carcinoembryonic antigen, labetuzumab, inhibits tumor growth and sensitizes human medullary thyroid cancer xenografts to dacarbazine chemotherapy. *Mol Cancer Ther* (2004); 3(12): 1559.

⁴⁴ Behr, et al. Improved treatment of medullary thyroid cancer in a nude mouse model by combined radioimmunotherapy: doxorubicin potentiates the therapeutic efficacy of radiolabeled antibodies in a radioresistant tumor type. *Cancer Res* (1997); 57(23): 5309.

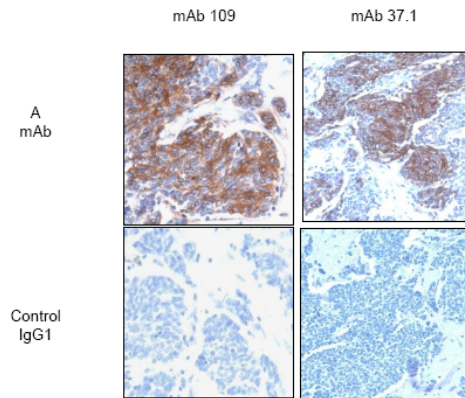
⁴⁵ Strickland LA, et al. Preclinical evaluation of carcinoembryonic cell adhesion molecule (CEACAM) 6 as potential therapy target for pancreatic adenocarcinomas. *J Pathol* (2009); Feb 27: epub ahead of print.

⁴⁶ Sharkey, RM, et al. A phase I trial combining high-dose ⁹⁰Y-labeled humanized anti-CEA monoclonal antibody with doxorubicin and peripheral blood stem cell rescue in advanced medullary thyroid cancer. *J Nucl Med* (2005); 46(4): 620.

⁴⁷ Liersch, T, et al. Update of carcinoembryonic antigen radioimmunotherapy with (131)I-labetuzumab after salvage resection of colorectal liver metastases: comparison of outcome to a contemporaneous control group. *Ann Surg Oncol* (2007); 14(9): 2577.

ICT-109 and ICT-37 may well have certain advantages over antibodies developed elsewhere. As shown in Figure 3, CEACAM5 and CEACAM6 are distributed differently, which means that the two antibodies may have distinct therapeutic uses.⁴⁸

Figure3. Immunohistochemical staining with ICT-109 and ICT-37.



Source: ImmunoCellular Therapeutics

Then, too, each monoclonal antibody is different, based upon the site on the antigen that is recognized and the binding characteristics of the antibody. Targeting CEACAM5 and CEACAM6 is that much more complex because these are glycoproteins and their antigenic sites are at least partially defined by their sugar moieties. As shown in Table 1, the antibodies created via the DIAAD technology exhibit very high affinities to their targets, even when compared against antibodies comprising approved medicines.

Table 1. A Comparison of Antibody Affinities.

MoAb	TARGET	TYPE	Kon	Koff	Kd
109	CAM5 and CAM6	IgG1	6.60e4	3.8e-5	580 ±20pM
37	CAM5	IgG2a	1.2227e5	4.9e-6	40 ±7 pM

Affinities of top monoclonal antibodies used in cancer

Product Name	Kd (nM)
Rituxan	8
Herceptin	5
Avastin	1.1
Erbixux	0.2

Source: ImmunoCellular Therapeutics

ImmunoCellular’s drug candidates also exhibit a high specificity to their targeted molecules, which should minimize the potential for off-target toxicities, and they display a significant inhibitory effect on tumor growth in a xenograft model.⁴⁹

⁴⁸ Blumenthal, RD, et al. Expression patterns of CEACAM5 and CEACAM6 in primary and metastatic cancers. BMC Cancer (2005); 7: 2.

⁴⁹ ImmunoCellular Therapeutics private communication.

The Company intends to continue its preclinical research of these two patent-protected therapies⁵⁰ for small cell lung and pancreatic cancer, but it is seeking a partner to pursue clinical development. (See the following box for an overview of small cell lung cancer.) Our estimates are based on an assumption that the two antibodies are outlicensed to the same partner, since they share a common target. Furthermore, we have assumed that clinical development commences in 2010, as the preclinical research should be completed in the second half of this year.

Small cell lung cancer is a disease with a well known cause, since cigarette smoking accounts for over 95% of all cases. As such, new diagnoses closely track long-term trends in smoking behavior, as exhibited in a decline in incidence from 17% to 13% of all lung cancers reported in United States over the past 30 years.²⁷ Nonetheless, small cell lung cancer inflicts a severe toll on humanity, for the disease typically starts in the central portion of the lung from which it rapidly metastasizes. Most patients (roughly 90%) have metastatic disease upon diagnosis and are not considered candidates for surgical resection. Moreover, the risk of death increases markedly from stage IA to stage IIA (1.5 fold), stage IIIA (1.9 fold), stage IVA (3.1 fold) and stage IVB (4.3 fold).⁵¹ First line therapy is typically etoposide and carboplatin, which have response rates of 77% and a median survival time of 15.3 months. Other chemotherapeutic regimens, including topotecan and irinotecan, have been substituted and modified dosing regimens, sometimes with additional drugs included, have been employed, but the median survival has largely remained less than 18 months. Radiation therapy has also been used, though local recurrence has been problematic. As a result, small cell lung cancer claimed the lives of more than 21,000 individuals in the United States alone last year.¹²

ICT-69 & THE DIAAD PLATFORM

Using this novel approach to generating disease-related antibodies, ImmunoCellular is working on another antibody with a high affinity and specificity for an antigen associated with multiple myeloma and ovarian cancer. The Company aims to have the antigen characterized later this year, which should enable the assembly of preclinical data to initiate partnering negotiations. We believe the company's extensive patent estate⁵² and preclinical data will lead to a deal in 2010 and that the therapeutic agent, ICT-69, will enter clinical trials a year later.

The success of the DIAAD technology to date suggests that ImmunoCellular has only just begun to employ this novel discovery platform. Oncology is the Company's primary area of interest, but antibodies have been used successfully for other indications, including serious infectious agents, inflammatory diseases, and degenerative disorders. Accordingly, the DIAAD platform probably will yield many more therapeutic agents for a broad range of maladies over time.

⁵⁰ One patent granted (US # 7,183,389), three allowed, and six pending.

⁵¹ Ou, SI and Zell, JA. The applicability of the proposed IASCLC staging revisions to small-cell lung cancer (SCLC) with comparison to the current AJCC6th TNM edition. Presented at the 2008 Chicago Multidisciplinary Symposium in Thoracic Oncology, November 13-15, 2008.

⁵² Three patents granted (US # 6,376,654; 6,986,891; and 7,226,750) and eight pending.



INTELLECTUAL PROPERTY

ImmunoCellular Therapeutics has assembled an intellectual property to protect its key technologies and drug candidates. The patent portfolio, which includes 14 patents issued and pending related to its “active” immunotherapy program, covers the composition of matter and the administration of dendritic cells that have been exposed to certain antigens to elicit a therapeutic immune response against various cancers, including gliomas. Key to this program are the following patent applications:

ICT-121	WO2008/039874 & US2008/0206286 (both published)	Provide methods and compositions for cancer vaccines that target cancer stem cells, including methods of treating cancer with a DC vaccine and inducing an immune response in a patient to preparations of various cancer stem cell antigens or synthetic peptide fragments of CD133 and other proteins.
ICT-121	CD133 patent filed	Composition of matter and use in a cancer vaccine
ICT-107	US2008/0311141 (published)	Use patent for immunizing glioma and glioblastoma patients with DCs loaded <i>in vitro</i> with unique combinations of multiple tumor antigens to induce a therapeutic immune response. Six specific antigens are mentioned: tyrosinase-related protein (TRP-2), melanoma-associated antigen-1 (MAGE-1), HER-2, IL-13, receptor α 2, gp100, and AIM-2.
ICT-107	US2008/0311142 (published)	Use of mutated antigen loaded into DCs that elicits an antigen-specific immune response more potent than that elicited by the native molecule.

The “passive” immunotherapy program is protected by 26 patents issued and pending that cover the composition of matter, use of its antibodies therapeutically against multiple myeloma, ovarian cancer, small cell lung cancer, and pancreatic cancer, and the use of its antibodies for diagnostic purposes. The key patents protecting this program are presented in the following table:

ICT-109 & ICT-37	US 7183389 (granted)	Use of monoclonal antibodies (mcAb) against cell surface antigens for the detection & treatment of small cell lung cancer (SCLC).
ICT-109 & ICT-37	US 7435415 (granted)	Method of inhibiting growth or killing SCLC cells in a patient with either the mcAb alone or conjugated with a cytotoxic agent, including a chemotherapeutic agent, photoactivated toxin, or radionuclide.
ICT-109 & ICT-37	US 7435554 (granted)	Method of detecting the presence or extent of SCLC in a patient’s tissue, bodily fluid, or cells by binding to proteins with specific characteristics including molecular weight, glycosylation, and location on the surface SCLC cells.



ICT-109 & ICT-37	US2009/0041660 (published)	Composition of matter patent on mcAb that recognizes an antigen present on the surface of pancreatic cancer cells and method of diagnosing or inhibiting/killing pancreatic cells in a patient with or without detectable or cytotoxic conjugates.
ICT-69	US 6376654 (granted)	Method of using mcAb and antibody fragments that bind to cell surface membranes of multiple myeloma and ovarian cancer cells for therapeutic, diagnostic, and cell purification purposes.
ICT-69	US 6986891 (granted)	Method of using mcAbs or antibody fragments for killing or inhibiting tumor cell growth in patients with multiple myeloma or ovarian cancer
ICT-69	US 7226750 (granted)	Method of detecting ovarian cancer in a patient or biological sample with a mcAb, antibody fragment, or either with a detectable moiety (e.g., fluorophore, chromophore, or radionuclide).
ICT-69	US 7498129 (granted)	Method of monitoring effectiveness of a therapy against multiple myeloma or ovarian cancer via mcAb or antibody fragment binding in a bodily fluid sample (e.g., blood, serum, or plasma).



INVESTMENT CONCERNS AND RISKS

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

- **Stock risk and market risk:** There is a limited trading market for the Company's common stock. There can be no assurance that an active and liquid trading market will develop or, if developed, that it will be sustained, which could limit one's ability to buy or sell the Company's common stock at a desired price. Investors should also consider technical risks common to many small-cap or micro-cap stock investments, such as small float, risk of dilution, dependence upon key personnel, and the strength of competitors that may be larger and better capitalized.
- **Competitive risk:** The pharmaceutical and biotechnology markets are rapidly evolving, and research and development are expected to continue at an accelerated pace. Other companies are also actively engaged in the development of therapies to directly or indirectly treat those disorders being pursued by ImmunoCellular. These companies may have substantially greater research and development capabilities, as well as significantly greater marketing, financial, and human resources than ImmunoCellular.
- **Products still in development phases:** The Company's products are still in the discovery stage. Such products may appear to be promising, but may not reach commercialization for various reasons, including failure to achieve regulatory approvals, safety concerns, and/or the inability to be manufactured at a reasonable cost. And even if its products are commercialized, there can be no assurance that they will be accepted, which may prevent the Company from becoming profitable.
- **Funding requirements:** It is difficult to predict ImmunoCellular's future capital requirements. The Company may need additional financing to continue funding the research and development of its products and to expand its business. There is no guarantee that it can secure the desired future capital or, if sufficient capital is secured, that current shareholders will not suffer significant dilution.
- **Regulatory risk:** There is no guarantee that ImmunoCellular's products will be approved by the U.S. Food and Drug Administration (FDA) or international regulatory bodies for marketing in the U.S. or abroad.
- **Patent risk:** The field of immunotherapies is at an early stage of development, and although ImmunoCellular has licensed and/or filed for numerous patents to secure its right to commercialize this technology and its antibody therapeutic agents, not all of these patents have been challenged, and therefore some may not protect the Company's rights adequately in a competitive marketplace.



FINANCIAL ANALYSIS

REVENUE SOURCES

Our revenue projections reflect the company's intent to develop ICT-121, and includes no contributions from ICT-107. The model is consistent with ImmunoCellular's goal to outlicense its two lead antibody drug programs, ICT-109/37 and ICT-69 at a preclinical stage of development. We have assumed that diagnostic tests related to the therapeutic programs are outlicensed to experienced partners in exchange for a low single-digit royalty rate and that they are launched coincidentally with the ICT-121 vaccine and antibody-based drugs.

ICT-121: Glioblastoma			
Year penetration starts	2014	Incidence	39500
Starting penetration rate	2%	Percent addressable	70%
Years between penetration start and peak	7	Market growth rate	1%
Peak penetration	30%	Price per patient	\$30,000
Duration of peak penetration in years	10	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	15%
Stage of development	Phase I	Probability of commercialization	10%

Key assumptions regarding the ICT-121 glioblastoma program:

- The glioblastoma market size is estimated by assuming that 75% of brain tumor deaths in the United States are attributable to glioblastoma and applying that incidence rate to the estimated population of persons living in "more developed countries," as defined by the United Nations.
- 70% of the patient population is eligible for the vaccine, reflecting a portion whose general health, stage of their disease, and/or state of their immune systems prevent use of this therapy.
- Clinical development of ICT-121 commences with an Investigational New Drug application in Q3, 2009, in keeping with one of the corporate goals for this year.
- The Phase I/II clinical trial involves 18 to 20 patients with glioma/glioblastoma, and it is completed in 18 months.
- A pivotal Phase II/III trial is conducted under Special Protocol Assessment agreement with the FDA, thereby reducing the regulatory risk.
- ImmunoCellular outlicenses ICT-121 to marketing partners on a geographic basis, in exchange for \$200 million of upfront and milestone payments, as well as a mid-teens royalty rate on its partners' sales.
- The trial results are sufficiently convincing for ICT-121 to gain a 6% share of the U.S. market in its first year. Subsequently, it enters foreign markets, reaching 30% the glioblastoma market in developed countries seven years after approval.



- The vaccine's average worldwide price is \$30,000. No provision is made for price hikes, due to uncertainty over the impact of healthcare reform programs.
- The probability of commercialization is set at 10%, based upon the vaccine's current stage of development and historical success rates for the development of therapeutic agents in the United States.

ICT-121: Pancreatic Cancer			
Year penetration starts	2016	Incidence	147400
Starting penetration rate	3%	Percent addressable	90%
Years between penetration start and peak	8	Market growth rate	2%
Peak penetration	20%	Price per patient	\$30,000
Duration of peak penetration in years	6	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	15%
Stage of development	Phase I	Probability of commercialization	10%

Key assumptions regarding the ICT-121 pancreatic cancer program:

- The size of the pancreatic cancer market reflects the number of new diagnoses in developed countries of the world.
- The addressable market is 90%, limited by the patient's general health, status of the immune system, and stage of the disease.
- The market is growing faster than the overall population in developed countries.
- Marketing partners launch ICT-121 in the United States in 2016, followed shortly thereafter in other countries.
- The vaccine's initial penetration rate of the pancreatic cancer market is 3%, rising to 20% after eight years. This reflects the potential of new therapies entering the market by late decade.
- The price of the therapy, royalty rate, and probability of commercialization are the same for pancreatic cancer as they are for glioblastoma.



ICT-109/037: Small Cell Lung Cancer			
Year penetration starts	2015	Incidence	96440
Starting penetration rate	7%	Percent addressable	75%
Years between penetration start and peak	8	Market growth rate	0%
Peak penetration	30%	Price per patient	\$30,000
Duration of peak penetration in years	6	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	7%
Stage of development	Preclinical	Probability of commercialization	6%

Key assumptions for ICT-109/37 program:

- ImmunoCellular outlicenses these antibodies as a package for development by marketing partners at a preclinical stage of development in exchange for upfront and milestone payments totaling \$50 million, as well as a 7% royalty rate on its partners' sales.
- The Phase I clinical trial begins by 2011 and takes 9 to 12 months to complete with patients suffering from small cell lung cancer.
- A Phase II/III clinical study takes 24 months to complete, supporting the drug's launch in developed countries in 2015.
- The penetration rate is 7% initially and rises to 30% eight years after the antibody's debut.
- The market size is estimated from the number of new lung cancer cases diagnosed in developed countries, adjusted to reflect the proportion (13%) accounted for by small cell lung cancer in the United States.
- The addressable market is 75%, limited by the general health of the patient and the stage of the cancer upon diagnosis.
- The probability of commercialization is 6%, based on the program's current stage of development.



ICT-069: Multiple myeloma			
Year penetration starts	2017	Incidence	79825
Starting penetration rate	5%	Percent addressable	50%
Years between penetration start and peak	8	Market growth rate	1%
Peak penetration	16%	Price per patient	\$25,000
Duration of peak penetration in years	5	Treatment price growth	0%
Retention rate in decline years	90%	Royalty rate	6%
Stage of development	Preclinical	Probability of commercialization	5%

Key assumptions regarding ICT-69:

- ImmunoCellular outlicenses this therapeutic antibody at a preclinical stage of development in 2010 in exchange for \$20 million in upfront and milestone payments, as well as a 6% royalty rate on its partners' sales.
- The clinical development program is initiated in 2011 and is completed roughly five years later, enabling commercialization in 2017.
- The initial penetration rate of 5% and the maximum penetration rate of 16% reflect the availability of alternative therapies for this disease.
- The patient population is based upon the incidence of multiple myeloma in the United States and applied to the estimated population of "more developed countries," as defined by the United Nations.
- The addressable market is 50%, based upon the use of genetic analyses and/or the related diagnostic test for ICT-69 to identify only patients who might benefit from the therapeutic antibody.
- A patient receives a year of therapy at an average price of \$25,000.
- The probability of commercialization is 5%, based on the status of this development program.



INCOME STATEMENT # (Fiscal year ends December 31st.)

	2009	2010	2011	2012	2013
Total revenue	\$ 1,000	\$ 2,200	\$ 8,400	\$ 15,300	\$ 16,300
COGS	-	-	-	-	-
Gross profit	\$ 1,000	\$ 2,200	\$ 8,400	\$ 15,300	\$ 16,300
Operating expenses					
R&D	\$ 1,500	\$ 1,500	\$ 2,500	\$ 6,000	\$ 6,000
Administrative					
General	1,000	1,500	2,000	2,000	2,000
Total expense	2,500	3,000	4,500	8,000	8,000
Operating profit	\$ (1,500)	\$ (800)	\$ 3,900	\$ 7,300	\$ 8,300
Non-operating income/expense					
Interest expense					
Interest income					
Other					
Total non-operating	-	-	-	-	-
Pretax profit	\$ (1,500)	\$ (800)	\$ 3,900	\$ 7,300	\$ 8,300
Income tax			1,482	2,774	3,154
Net income	\$ (1,500)	\$ (800)	\$ 2,418	\$ 4,526	\$ 5,146
Earnings (loss) per share	\$ (0.12)	\$ (0.06)	\$ 0.17	\$ 0.31	\$ 0.33
Diluted shares outstanding	12750	13000	14250	14500	15500

*All figures are in thousands, except per-share data.

Key assumptions regarding the income statement:

- All upfront and milestone payments are recognized over five-year periods.
- Since we've assumed that ImmunoCellular outlicenses its products, we've made no provisions for manufacturing or marketing costs.
- Administrative expenses include royalties paid for inlicensed intellectual property.



April 27, 2009

- R&D costs in 2009 approximate the \$1.3 million invested in 2008. Thereafter, they rise as ICT-121 enters more advanced clinical trials. By 2014, new product development costs reach 19% of revenues, a level that is maintained thereafter.
- General expenses in 2009 total \$1 million, or 70%-75% of the level incurred last year. Over time, these expenses increase as the corporate infrastructure expands to support the development of ICT-121 and its commercialization. Thereafter, we've assumed the company devotes 8% of its revenues to these operating items.
- The corporate effective tax rate is 38%, and no provision is made for net operating loss carryforwards.
- We've assumed that exercising of options gradually increases the number of shares outstanding.



BALANCE SHEET #

ASSETS	12/31/2008
Current Assets	
Cash & equivalents	3,085
Other	28
Total Current Assets	\$ 3,113
Property & equipment	\$ 8
Intangible assets	-
Other	7
Total Assets	\$ 3,128
LIABILITIES	
Current Liabilities	
Accounts payable	\$ 133
Debt due	-
Other	55
Total Current Liabilities	\$ 188
Long-term debt	\$ -
Shareholders Equity	
Common Stock, par value	\$ 13
Additional Paid-In Capital	15,012
Accumulated Deficit	(12,085)
Treasury Stock	-
Total Shareholders Equity	\$ 2,940
Total liabilities & equity	\$ 3,128

All figures are in thousands.



DISCOUNTED CASH FLOW ANALYSIS #

	2009	2010	2011	2012	2013
Revenue	\$ 1,000	\$ 2,200	\$ 8,400	\$ 15,300	\$ 16,300
Operating income	-1500	-800	3900	7300	8300
Net income	-1500	-800	2418	4526	5146
Depreciation/amortization	2	3	3	10	10
Stock-based compensation	500	500	500	600	600
Tax loss carryforwards	0	0	0	0	0
Capital expenditures	0	-1	-2	-25	-25
Asset purchases					
Other					
Total cash flow adjustments	502	502	501	585	585
Free cash flow	\$ (998)	\$ (298)	\$ 2,919	\$ 5,111	\$ 5,731
Risk-adjusted free cash flow	\$ (998)	\$ (298)	\$ 275	\$ 487	\$ 548

Discount Rate	Discounted Cash Flows (2008 - 2024)	PV of Terminal Value at a					
		Perpetual growth rate of rFCF			Enterprise Value		
		2.0%	3.0%	4.0%	2.0%	3.0%	4.0%
7.5%	\$26,113.10	\$ 66,381	\$ 81,927	\$ 106,358	\$92,494	\$108,040	\$132,471
10.0%	\$19,701.87	\$ 32,326	\$ 37,306	\$ 43,946	\$52,028	\$57,008	\$63,648
12.5%	\$14,989.65	\$ 17,581	\$ 19,623	\$ 22,144	\$32,571	\$34,612	\$37,134
15.0%	\$11,489.55	\$ 10,212	\$ 11,172	\$ 12,306	\$21,702	\$22,661	\$23,795
17.5%	\$8,863.48	\$ 6,203	\$ 6,696	\$ 7,262	\$15,067	\$15,560	\$16,126

Discount Rate	Net Debt	Total Equity Value			Value per Diluted Share		
		2.0%	3.0%	4.0%	2.0%	3.0%	4.0%
		7.5%	\$ (3,085)	\$95,579	\$111,125	\$135,556	\$ 6.17
10.0%	(3,085)	\$55,113	\$60,093	\$66,733	\$ 3.56	\$ 3.88	\$ 4.31
12.5%	(3,085)	\$35,656	\$37,697	\$40,219	\$ 2.30	\$ 2.43	\$ 2.59
15.0%	(3,085)	\$24,787	\$25,746	\$26,880	\$ 1.60	\$ 1.66	\$ 1.73
17.5%	(3,085)	\$18,152	\$18,645	\$19,211	\$ 1.17	\$ 1.20	\$ 1.24

Discount Rate	Terminal Value as % Enterprise Value			Implied EBITDA Multiple		
	2.0%	3.0%	4.0%	2.0%	3.0%	4.0%
	7.5%	71.8%	75.8%	80.3%	11.67	14.41
10.0%	62.1%	65.4%	69.0%	8.02	9.26	10.91
12.5%	54.0%	56.7%	59.6%	6.11	6.82	7.70
15.0%	47.1%	49.3%	51.7%	4.94	5.40	5.95
17.5%	41.2%	43.0%	45.0%	4.14	4.47	4.85

All figures are in thousands, except per-share data.



Assumptions related to the Discounted Cash Flow Analysis:

- The DCF model projects cash flow through 2024, discounted back at multiple annual rates (7.5%, 10.0%, 12.5%, 15.0%, and 17.5%) to demonstrate the potential variability related to this assumption. It also includes three perpetual growth rates (2%, 3%, and 4%) to show the impact on the present value of the company's terminal value. The rates used in calculating the per-share value for ImmunoCellular are a 12.5% annual discount rate and a perpetual growth rate of 3%. The number of fully-diluted shares estimated to be outstanding in 2013, 15.5 million, is used in the per-share calculation.
- The cash flows are risk adjusted, based on the proportional gross profit contribution by each therapy on an annual basis and the probability of that therapy being commercialized. For any years in which we are projecting losses, the probability is conservatively set at 100%.

TRANSACTIONS ANALYSIS

The value of a biotechnology company and its assets is a function of both the commercial potential of the drugs under development and the environment in which it is operating. Over the past six to nine months, the world markets have been shaken to their core by upheaval in the financial sector and a spillover to the general economy. To consider the value of ImmunoCellular within this environment, we reviewed acquisitions and licensing deals in the pharmaceutical and biotechnology industries and selected deals that involved biological products and oncology therapies at early stages of development (up to, but not through Phase II clinical trials). The deals, which are presented in the table below, involved products consisting of traditional small molecules, antibodies, and vaccines.

Table 2. Recent Biotech/Pharmaceutical Acquisitions

Target Company	Acquirer/Licensee	Date	Technology/R&D Pipeline	Price (in mill.)	Price per Drug
Virosome Biologicals	Mymetics	Mar-09	2 vaccine candidates	\$22.2	\$11.1
Arana Therapeutics	Cephalon	Feb-09	5 antibodies for oncology & autoimmune dis	\$163.4	\$32.7
Dynavax	GlaxoSmithKline	Dec-08	4 drug programs targeting toll-like receptors	\$210.0	\$26.3
GemVax	Vaxonco	Oct-08	Dendritic cell vaccine	\$11.4	\$11.4
Neose Technologies	Novo Nordisk	Sep-08	Preclinical drugs - oncology & hematology	\$21.0	\$21.0
Average Transaction Value:				\$85.6	
Average Price per Drug:					\$20.5

The deals range in size from \$11.4 million to \$210 million, reflecting the perceived value of the technologies and the number of compounds being acquired. In the cases in which more than one drug was involved, we divided the acquisition price by the specific number of drugs to calculate a per-drug valuation. In the Dynavax – GlaxoSmithKline deal, we assumed that each program would yield two drugs, given the multiple applications possible for toll-like receptor therapies.

Based on the average price paid per drug shown in Table 2, we calculated the value of ImmunoCellular Therapeutic’s R&D pipeline without regard to the sizes of the potential markets or levels of competition that each drug might face. We assumed that each project will be outlicensed at the end of the years described in the Clinical Applications section and the drugs’ values were discounted back at a 30% annual rate to mid-2009. The comparative transaction analysis yields a value of \$39.6 million, or \$3.12 per basic IMUC share. The elements of our calculation are presented in Table 3:

Table 3. Valuation of ImmunoCellular’s R&D pipeline

IMUC Drug	Est'd Deal Date	Present Value*
ICT-121	2012	\$8.1
ICT-109/037	2009	\$17.8
ICT-069	2010	\$13.7
Total PV:		\$39.6
PV per IMUC share:		\$3.12

** All figures in millions, except per-share amount.*



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ImmunoCellular Therapeutics common stock trades on OTCBB under the symbol "IMUC"

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