Ocean Biomedical (NASDAQ: OCEA) Celebrates Discovery of Bispecific Antibodies and Immune Checkpoint Inhibitors That Kill Glioblastoma Cells and Melanoma Cells, and Block the Metastasis of Malignant Melanoma Cells to the Lung by Over 90%

February 23, 2023

Providence, RI, Feb. 23, 2023 (GLOBE NEWSWIRE) -- As previously announced, Ocean Biomedical, Inc. (NASDAQ: OCEA) celebrates the discovery of **bispecific antibodies** that target Chitinase 3-like-1 and immune checkpoint inhibitors, **killing glioblastoma cells and melanoma cells, and blocking the metastasis of malignant melanoma cells to the lung by over 90%.** Glioblastoma multiforme (GBM) is a deadly type of brain tumor and 5-year survival is just 8% for those aged 45-54. About 25% of GBM patients are not actively treated due to rapid disease progression. Malignant melanoma, the most serious skin cancer, can metastasize to other organs. Once it has spread to other organs it is difficult to treat. Metastatic melanoma (Stage IV) has 22.5% five year survival. Non-small cell lung cancer (NSCLC) is a major unmet medical need that accounts for 85% of pulmonary malignancies and effects approximately 450,000 individuals. In greater than 50% of affected patients the tumors are diagnosed at advanced stages with metastatic spread that precludes curative surgical resection.

Background

Recent studies of NSCLC have highlighted genetic abnormalities that underlie these tumors. These genetic abnormalities generate abnormal proteins that have not been previously seen by the patient's immune system which, in turn, activates antitumor immune responses that control tumor initiation and progression. Studies over recent years have demonstrated that tumor initiation and progression are often mediated by the ability of the tumors to produce immunosuppressive proteins and activate immunosuppressive pathways, called immune checkpoint inhibitors (ICPI), that allow tumor growth and progression by shutting off these critical anti-tumor immune responses. This includes the programed death (PD) pathway including PD-1, PD ligand 1 (PD-L1) and PD-L2 and the cytotoxic T-lymphocyte-associated protein 4 (CTLA4) pathway that includes CTLA4 and its binding partners B7.1/B7.2. Antibodies that target ICPI such as PD-1, PD-L1 and CTLA4 have been generated which have therapeutic efficacy in NSCLC and other tumors. Unfortunately, only a minority of patients respond to these therapies and the responses are often not durable.

Chitinase 3-like-1 (CHI3L1) is a member of the 18 glycosyl hydrolase gene family that is readily detected in the circulation of normal individuals and expressed at exaggerated levels in the circulation of individuals with diseases characterized by inflammation, tissue remodeling and or cancers.

Discoveries

Recent studies from our laboratory have demonstrated that CHI3L1 is a critical regulator of a number of key cancer-causing pathways. We have highlighted its ability to inhibit tumor cell death (apoptosis), its inhibition of the expression of the tumor suppressors P53 and PTEN and its stimulation of the B-RAF protooncogene. Most recently we have discovered that CHI3L1 is a "master regulator" of ICPI including key elements of the PD-1 and CTLA4 pathways. In accord with the importance of these pathways we have also generated antibodies: 1.) a **monoclonal antibody against CHI3L1**, and 2.) **bispecific antibodies that simultaneously target CHI3L1 and PD-1 or CTLA4**. The impressive ability of our bispecific antibodies to control primary and metastatic lung cancer in murine experimental modeling systems is discussed below.

We generated **bispecific antibodies that simultaneously target CHI3L1 and PD-1 or CTLA4**. We then compared their effects in experimental models in which T cells and tumor cells are cultured together (a co-culture system) and in a murine model of lung metastasis. In all cases we compared the effects of the bispecific antibody to control antibodies, and to individual monospecific antibodies against CHI3L1, PD-1 or CTLA4, alone or in combination and the results are shown in the figures below.

In the coculture system, critical immune regulating cells called T cells were placed in culture with cancer cells. The ability of the antibodies to induce T cell differentiation and kill (induce apoptosis) of the tumor cells were then evaluated. As can be seen in Figure 1 below, tumor cell death was not induced by isotype control antibodies, and modest degrees of tumor cell apoptosis were seen in cultures with monospecific antiCHI3L1, antiPD-1 or antiCTLA4 individually. Additive tumor cell death was seen when antiCHI3L1 was administered in combination with antiPD-1 or and CTLA4 alone. Most importantly, highly impressive synergistic tumor cell death was seen when the cocultures were treated with the bispecific antibodies (FRGxCTLA4 or FRGxPD-1). In all cases the cell death that was induced was due to T cell differentiation into CD8+ cytotoxic T cells.

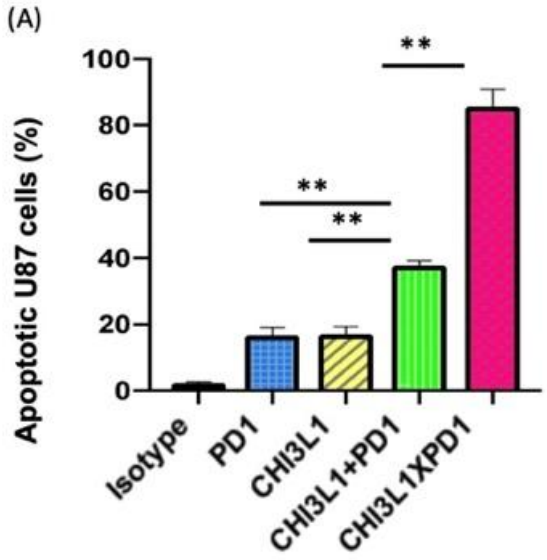

Fig. 1. Characterization of cell death (Apoptosis) responses induced in U87 glioblastoma cells in cocultures with T cells treated with isotype control antibody (black), antiPD-1 monospecific antibody (blue), antiCHI3L1 monospecific antibody (yellow), antiCHI3L1 and antiPD-1 in combination (green) and the CHI3L1xPD-1 bispecific antibody (magenta).

In the murine metastasis model we administered malignant melanoma cells into the murine circulation and evaluated their spread to the lungs and pleural surface by counting the number of black staining pleural metastasis. Tumor metastasis were readily appreciated in lungs from mice treated with isotype control antibodies, and modest decreases in metastasis were seen in lungs from mice treated with monospecific antiCHI3L1, antiPD-1 or antiCTLA4 individually. Additive inhibition of tumor spread was seen when antiCHI3L1 was administered in combination with antiPD-1 and CTLA4. Most importantly, highly impressive synergistic inhibition of tumor metastasis was seen in lungs from mice treated with the bispecific antibodies (FRGxCTLA4 or FRGxPD-1). Figure 2 below shows the results with the FRGxCTLA4 antibody.

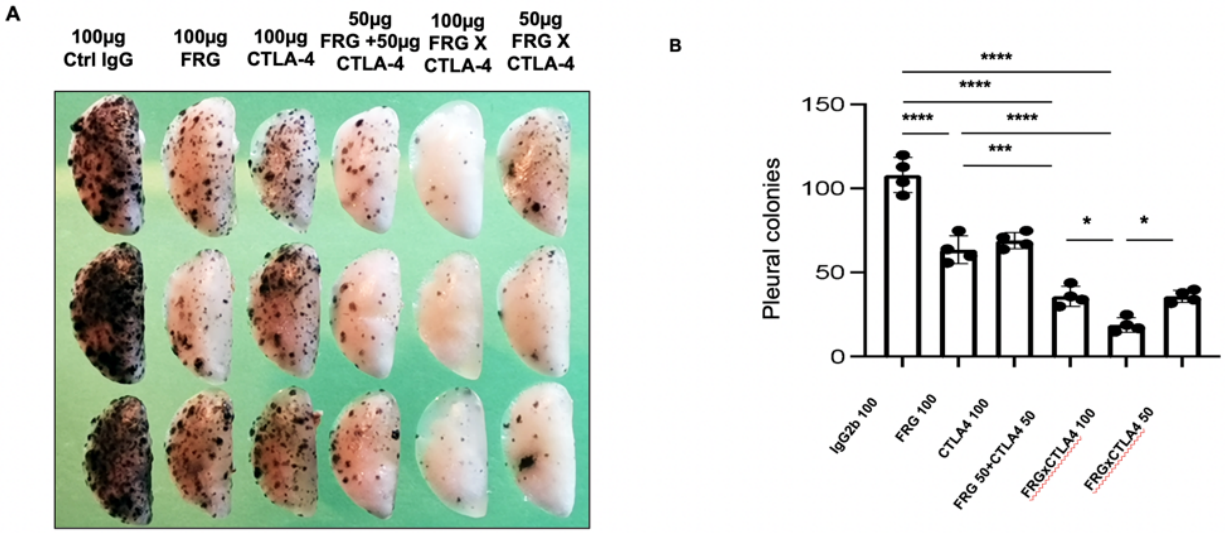

Fig.2. Mice were treated with malignant melanoma cells and then the noted antibody or antibody combinations. Metastasis cause black dots on the lung pleural surface which are illustrated on the left and quantitated on the right. The effects of Anti-Chi3l1 (FRG) and anti-CTLA4, alone and in combination and bispecific antibody that targets CHI3L1 and CTLA4 (FRGxCTLA4) are compared. *** P<0.001; ****P<0.0001

Quoted

“Bispecific antibodies that simultaneously target CHI3L1 and ICPI like PD-1 and or CTLA4 have an impressive and synergic ability to induce tumor cell death and prevent tumor metastasis compared to individual antibody moieties,” commented Dr. Jack A. Elias, Dean Emeritus of Medicine and Biological Sciences and Professor of Translational Science, Medicine and Molecular Microbiology and Immunology at the Warren Alpert Medical School Brown University; Scientific co-founder.

“Non-small cell lung cancer (NSCLC) is the leading cause of cancer death and second most diagnosed cancer in the US. Glioblastoma multiforme (GBM) is a lethal type of brain tumor that affects approximately 28,000 people in the U.S. The median survival time is about 15 months. With our discovery that CHI3L1 is a critical regulator of a number of key cancer-causing pathways by highlighting its ability to inhibit tumor cell death (apoptosis) this therapy has the potential to save thousands of lives of people effected from NSCLC and GBM,” said Dr. Chirinjeev Kathuria, co-founder and Executive Chairman.

Suren Ajjarapu, one of Ocean’s Directors commented, “Ocean is proud to be advancing this exciting discovery and we look forward to bringing these therapies to patients. This discovery and others will lead to long term shareholder value growth and appreciation.”

About Ocean Biomedical

Ocean Biomedical, Inc. is a Providence, Rhode Island-based biopharma company with an innovative business model that accelerates the development and commercialization of scientifically compelling assets from research universities and medical centers. Ocean Biomedical deploys the funding and expertise to move new therapeutic candidates efficiently from the laboratory to the clinic, to the world. Ocean Biomedical is currently developing five promising discoveries that have the potential to achieve life-changing outcomes in lung cancer, brain cancer, pulmonary fibrosis, and the prevention and treatment of malaria. The Ocean Biomedical team is working on solving some of the world’s toughest problems, for the people who need it most.

To learn more, visit www.oceanbiomedical.com

Forward-Looking Statements

The information included herein and in any oral statements made in connection herewith include “forward-looking statements” within the meaning of the “safe harbor” provisions of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by the use of words such as “estimate,” “plan,” “project,” “forecast,” “intend,” “will,” “expect,” “anticipate,” “believe,” “seek,” “target” or other similar expressions that predict or indicate future events or trends or that are not statements of historical matters, although not all forward-looking statements contain such identifying words. These forward-looking statements include, but are not limited to, statements regarding estimates and forecasts of financial and performance metrics and expectations. These statements are based on various assumptions, whether or not identified herein, and on the current expectations of the Company’s management and are not predictions of actual performance. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as, and must not be relied on by any investor as, a guarantee, an assurance, a prediction or a definitive statement of fact or probability. Actual events and circumstances are difficult or impossible to predict and will differ from assumptions.

The announced discoveries were based solely on laboratory and animal studies. Ocean Biomedical has not conducted any studies that show similar efficacy or safety in humans. There can be no assurances that this treatment will prove safe or effective in humans, and that any clinical benefits of this treatment is subject to clinical trials and ultimate approval of its use in patients by the FDA. Such approval, if granted, could be years away.

Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties. These forward-looking statements are not guarantees of future performance, conditions or results, and involve a number of known and unknown risks, uncertainties, assumptions and other important factors, many of which are outside the control of the Company that could cause actual results or outcomes to differ materially from those discussed in the forward-looking statements. Important factors, among others, that may affect actual results or outcomes include (i) the outcome of any legal proceedings that may be instituted against the Company; (ii) changes in the markets in which the Company competes, including with respect to its competitive landscape, technology evolution, or regulatory changes; (iii) changes in domestic and global general economic conditions; (iv) risk that the Company may not be able to execute its growth strategies; (v) risks related to the ongoing COVID-19 pandemic and response, including supply chain disruptions; (vi) risk that the Company may not be able to develop and maintain effective internal controls; (vii) the risk that the Company may fail to keep pace with rapid technological developments to provide new and innovative products and services or make substantial investments in unsuccessful new products and services; (viii) the ability to develop, license or acquire new therapeutics; (ix) the risk that the Company will need to raise additional capital to execute its business plan, which may not be available on acceptable terms or at all; (x) the risk that the Company experiences difficulties in managing its growth and expanding operations; (xi) the risk of product liability or regulatory lawsuits or proceedings relating to the Company’s business; (xii) the risk of cyber security or foreign exchange losses; (xiii) the risk that the Company is unable to secure or protect its intellectual property.

The foregoing list of factors is not exhaustive. You should carefully consider the foregoing factors and the other risks and uncertainties that are described in the Company’s Annual Report on Form 10-K for the year ended December 31, 2021 and its Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, and which are described in the “Risk Factors” section of the Company’s definitive proxy statement filed by the Company on January 12, 2023, and other documents to be filed by the Company from time to time with the SEC and which are and will be available at www.sec.gov. These filings identify and address other important risks and uncertainties that could cause actual events and results to differ materially from those contained in the forward-looking statements. Forward-looking statements speak only as of the date they are made. Readers are cautioned not to put undue

reliance on forward-looking statements, These forward-looking statements should not be relied upon as representing the Company's assessments as of any date subsequent to the date of this filing. Accordingly, undue reliance should not be placed upon the forward-looking statements.

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