June 6, 2023

Intensity Therapeutics Reports INT230-6 Can Cause Immune Priming in Historically Quiescent Breast Cancers

INT230-6 Induced T-Cell Receptor Signaling, Macrophage Markers, and IL-18 and B-Cell Receptor Signaling

Data Was Presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting on June 4, 2023

WESTPORT, Conn., June 6, 2023 /PRNewswire/ -- **Intensity Therapeutics, Inc.** ("Intensity"), a clinical-stage biotechnology company focused on the discovery and development of proprietary, novel immune-based intratumoral (IT) cancer therapies designed to kill tumors and increase immune system recognition of cancers, today announced that data from its INVINCIBLE study was presented on June 4, at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting being held in Chicago and virtually from June 2-6, 2023.

The INVINCIBLE study is a phase 2, randomized, open label, multi-center study that enrolled 91 women with newly diagnosed operable early-stage intermediate or high-grade T1-T2 invasive breast cancers who were randomly allocated (2:1) prior to resection to IT injections of INT230-6, no treatment or saline sham injection. The study is evaluating clinical and biological effects in patients with early-stage operable breast cancer. The study presented new immune and gene activation related results as well as data demonstrating efficacy and tolerability of INT230-6.

Abstract Title: A *phase 2 randomized window of opportunity trial evaluating cytotoxic and immunomodulatory effects of intratumoral INT230-6 in early stage breast cancer: The INVINCIBLE Trial.*
First Author: Angel Arnaout, MD, FACS
Session Type/Title: Poster Session/Breast Cancer—Local/Regional/Adjuvant
Session Date and Time: Sunday, June 4, 2023, 9:00 AM - 12:00 PM EDT
Location: In-Person & On Demand
Abstract Number: 573
Poster: 403

Copies of the presentation materials are available on Intensity'swebsite on the publications, papers and posters page.

"For the majority of breast cancer patients, the typical waiting period of 2-6 weeks from diagnosis to surgery is a very fearful time. Surgeons and patients feel powerless, as there are currently no therapeutic options for the patient prior to the surgery," said Angel Arnaout, M.D., Scientist and Surgical Oncologist at the Ottawa Hospital, and Professor of Surgery at

the University of Ottawa and Co-lead of the Ontario Institute for Cancer Research (OICR) WOO Network. "We have previously reported that the active drug agents comprising INT230-6 cause tumor cell death and high levels of necrosis in multiple breast cancer subtypes including triple negative breast cancer following direct intratumoral injection. The ability, with just one or two doses of this agent, to elicit a rapid and marked cytotoxic and immune induction response within the tumor during the surgical waiting period, all without an increase in postoperative complications, is very novel and highly attractive to patients. For the first time, there is the possibility that patients will have a treatment that can ignite the immune system prior to lumpectomy or mastectomy that may protect the patient from disease recurrence. We look forward to future studies to demonstrate that INT230-6 intratumoral injections can create a positive, long term clinical benefit for patients with breast cancer. As a surgeon, I am excited about how this new drug may shift the way we treat all cancer patients awaiting surgery, in general."

"From Part 2 of our study, we saw an increase in expression levels of dendritic cells, macrophages and CD4 T cells, post treatment, when comparing patients treated with drug with the control group," said Dr. Melanie Spears, Co-Director of Diagnostic Development, OICR and Co-lead of the WOO Network. "The cell death activates an anti-cancer immune response as evidenced by relative increase in the abundance of CD4 T naïve, B and NK cells, post treatment when comparing treated patients with the control group. Further work is currently in process to determine whether a global immune activation has occurred."

"INT230-6 has novel mechanism of action and is a potential, new weapon in the war on cancer. This drug can cause extensive necrosis with favorable clinical results as a monotherapy in presurgical and metastatic patients with advanced, relapsed and refractory disease," stated Lewis H. Bender, President and Chief Executive Officer of Intensity. "These new results reported from the INVINCIBLE breast cancer study provide further evidence and support for the potential of our drug in treating local disease prior to surgery. Specifically, the data from Part 2 of the INVINCIBLE study show that INT230-6 elicits both rapid direct tumor killing and immune activating effects. Having completed enrollment, we look forward to concluding the analysis and reporting the full patient study results in the future."

About INT230-6

INT230-6, Intensity's lead proprietary investigational product candidate, is designed for direct intratumoral injection. INT230-6 was discovered using Intensity's proprietary DfuseRx℠ technology platform. The drug is composed of two proven, potent anti-cancer agents, cisplatin and vinblastine, and a penetration enhancer molecule (SHAO) that helps disperse the potent cytotoxic drugs throughout tumors for diffusion into cancer cells. These agents remain in the tumor resulting in a favorable safety profile. In addition to local disease control, direct killing of the tumor by INT230-6 releases a bolus of neoantigens specific to the patient's malignancy, leading to engagement of the immune system and systemic anti-tumor effects. Importantly, these effects are mediated without the immunosuppression of concomitant systemic chemotherapy.

About the INVINCIBLE Study

The INVINCIBLE study is a phase 2, randomized, open label, multi-center study, that enrolled 91 women with newly diagnosed operable early-stage intermediate or high-grade T1-T2 invasive breast cancers who were randomly allocated (2:1) prior to resection to IT injections of INT230-6, no treatment or saline sham injection. The study had two parts. Part

1 (N=29) randomized patients 2:1 to either 1-3 doses of INT230-6 injected weekly or no treatment, 2 to 5 weeks prior to surgery (lumpectomy or mastectomy). The purpose of this portion of the trial was to evaluate safety, feasibility, and optimal drug dosing. Part 2, now complete, was a double-blind, randomized arm of 62 patients, where patients were randomized 2:1 to receive one or two IT doses of INT230-6 vs. saline injection. The objective of using saline was to rule out the potential confounding effect of hydrostatic pressure on tumor necrosis. The results of Part 2 further evaluated the potential cytotoxic, immunomodulatory and other biologic effects of INT230-6 and its role as a potential cancer therapy in breast cancer patients awaiting surgery. The INVINCIBLE Study is being conducted under a Health Canada (HC) approved Clinical Trial Application (CTA), under the direction and supervision of Principal Investigator, Dr. Angel Arnaout. The Ottawa Hospital Research Institute (OHRI) conducted subject enrollment and treatment, and evaluated pathological and clinical responses. OICR will analyze subject immune responses and conduct biomarker analyses.

About Potential INT230-6 Approval Pathways in the Presurgical Setting
The U.S Food and Drug Administration (FDA) instituted its Accelerated Approval Program to allow for earlier approval of drugs that treat serious conditions, and that fill an unmet medical need based on a surrogate endpoint. Pathological complete response (pCR) is an accepted FDA accelerated approval criterion for approval in high-risk breast cancer, such as TNBC subtype. Pathological complete response is defined as the absence of residual invasive and in situ cancer after evaluation of the complete resected breast specimen and lymph nodes following completion of neoadjuvant systemic therapy.

Data from the INVINCIBLE study has provided an understanding of the effect of INT230-6 on cancer cell proliferation and tumor necrosis. INT230-6 causes increased tumor necrosis with good safety, and the addition of INT230-6 to the existing or a modified neoadjuvant (presurgical) systemic standard-of-care treatment regimen may increase pCR rates in TNBC or HER+ patients. In November of 2020, Intensity Therapeutics met with FDA and discussed the potential use of INT230-6 in the presurgical neoadjuvant breast cancer setting in an accelerated approval program. A new meeting with the FDA is being planned.

About Intensity Therapeutics' Clinical Studies
INT230-6 has completed enrollment of over 200 patients in two phase 2 and phase 1 dose escalation clinical trials (NCT03058289 and NCT04781725) with various advanced solid tumors, IT-01 in metastatic disease, and IT-02 the INVINCIBLE study in presurgical breast cancer. The Company has a clinical collaboration agreement with Merck Sharpe & Dohme (Merck) to evaluate the combination of INT230-6, Intensity's lead product candidate, and KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 (programmed death receptor-1) therapy, in patients with advanced pancreatic, colon, squamous cell and bile duct malignancies. The Company also has a clinical collaboration agreement with Bristol-Myers Squibb to evaluate the combination INT230-6 with Bristol-Myers Squibb's anti-CTLA-4 antibody, Yervoy® (ipilimumab), in patients with advanced liver, breast and sarcoma cancers. Intensity is managing the individual combination arms separately with each respective partner via a joint development committee. The Company also executed agreements with the OHRI and OICR to study INT230-6 in the INVINCIBLE study, a randomized controlled neoadjuvant phase 2 study in women with early stage breast cancer.

About Intensity Therapeutics

Intensity Therapeutics, Inc. is a clinical-stage biotechnology company pioneering a new immune-based approach to treat solid tumor cancers. Intensity leverages its DfuseRx℠ technology platform to create new, proprietary drug formulations that, following direct injection, rapidly disperse throughout a tumor and diffuse therapeutic agents into cancer cells. Intensity's product candidates have the potential to induce an adaptive immune response that not only attacks the injected tumor, but also non-injected tumors. In addition to the clinical collaborations, the Company executed a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute's (NCI) Vaccine Branch. For more information, please visit www.intensitytherapeutics.com or follow the Company on Twitter @IntensityInc.

Forward-Looking Statements
This press release contains forward-looking statements regarding Intensity Therapeutics' plans, future operations and objectives. Such statements involve known and unknown risks, uncertainties and other factors that may cause actual performance or achievements to be materially different from those currently anticipated. These forward-looking statements include, among other things, statements about the initiation and timing of future clinical trials.

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