June 2, 2021

Intensity Therapeutics' INT230-6 Demonstrates Efficacy as Either Monotherapy or in Combination with Checkpoint Inhibitors in Patients with Relapsed, Refractory, Metastatic Solid Tumors

- *INT230-6 monotherapy overall showed an estimated 62% survival at one year,*
- *Patients receiving a dose of INT230-6 alone ≥50% of their tumor burden demonstrated a one-year survival estimate of 78%,*
- *Combined with pembrolizumab the one-year median overall survival estimate was 88%,*
- *Median overall survival of 23.6 months was observed in a heavily pre-treated mixed sarcoma population,*
- *Abscopal effects observed in multiple deep and distal tumors with biomarker changes demonstrating distal immune activation using INT230-6 monotherapy,*
- *All regimens were well tolerated with low rates of Grade 3 (12% monotherapy, 21% with Pembrolizumab) no Grade 4 or 5 adverse events,*

Full set of results to be presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting

WESTPORT, Conn.--(BUSINESS WIRE)-- Intensity Therapeutics, Inc. ("Intensity"), a clinical-stage biotechnology company developing proprietary, intratumoral products to kill tumors and increase immune system recognition of cancers, today announced data from its on-going Phase 1/2 clinical trial in refractory patients demonstrating efficacy and tolerability of INT230-6, either as monotherapy or in combination with checkpoint inhibitors (pembrolizumab or ipilimumab), in patients with relapsed, refractory and metastatic solid tumors. These posters will be presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting being held virtually from June 4 to 8.

"INT230-6 is our novel, proprietary, locally-delivered anti-cancer product candidate that has shown favorable clinical results as monotherapy in a basket study of patients with advanced and refractory disease," said Lewis H. Bender, President and CEO of Intensity Therapeutics. "The results of these studies to be presented at ASCO provide increased evidence and support of the potential of INT230-6. The data in the first poster show that INT230-6, either as monotherapy or in combination with pembrolizumab, is well tolerated and elicits both direct tumor killing and abscopal effects. The second presentation reports similar results of INT230-6 with or without ipilimumab in patients with advanced sarcoma, a cancer type with high unmet medical need."

INT230-6 +/- pembrolizumab

Title: *A Phase 1/2 Study of Intratumoral INT230-6 Alone (IT-01) or in Combination with Pembrolizumab [KEYNOTE-A10] in Adult Subjects with Locally Advanced, Unresectable and Metastatic Solid Tumors Refractory to Therapy*
Authors: El-Khoueiry, A.B., et al.
Session: Developmental Therapeutics - Immunotherapy
Session type: Poster Session
Abstract: 2592

The poster reports results from 72 subjects on the preliminary efficacy and safety of either INT230-6 alone (n=58) or in combination with the anti-PD-1 antibody, pembrolizumab (n=14) from an ongoing open-label Phase 1/2 clinical trial. Patients had a variety of relapsed, refractory metastatic solid tumors and progressed following a median of three prior therapies. INT230-6 was administered intratumorally every two weeks for five doses either alone or with 200 mg pembrolizumab dosed every three weeks. Preliminary efficacy results such as disease control rate and median overall survival (mOS) are being reported. Additional outcome measures included overall safety, and the pharmacokinetic profile.

Sixty-two percent of INT230-6 monotherapy subjects were alive at one year and median OS was not reached with 221 days of median follow-up. When the dose of INT230-6 relative to the subject's tumor burden (TB) was analyzed, subjects receiving a dose ≥50% of TB had not reached mOS with a median of 342 days of follow up (estimated to be 78% one-year OS). Subjects receiving a dose <50% of TB had an mOS of 95 days. This survival result achieved using INT230-6 compares favorably to historical survival data using the Royal Marsden Hospital Index (RMHI), a validated score that uses 3 incoming enrollment criteria to assess a patient's likelihood of survival in phase 1 basket studies (*Cancer* 2012;118:1422–8). One year survival of the INT230-6 with pembrolizumab combination arm was 88%; however, these data are still maturing.

There were nine patients in the monotherapy arm that demonstrated abscopal effects (i.e., shrinkage of multiple non-injected tumors). Together with the immunohistochemistry biomarker findings, the results suggest a systemic immune system activation. Eight of these nine monotherapy patients received an INT230-6 dose ≥50% of the TB further emphasizing the importance of proper dosing.

INT230-6, either as monotherapy or in combination with pembrolizumab, was well tolerated. The most common adverse events (AEs) were localized tumor-related pain, nausea, fatigue and vomiting. AEs were mainly mild to moderate with no Grade 4 or 5 AEs.

"Despite significant innovation in immunotherapeutic and checkpoint inhibitor therapy approaches for cancer treatment, patients with metastatic and refractory disease continue to have poor survival and response rates remain low in most tumor types," said Anthony B. El-Khoueiry, M.D., Director of the Phase I Program and Associate Professor of Clinical Medicine, Keck School of Medicine of the University of Southern California (USC). Dr. El-Khoueiry is also an oncologist at the USC Norris Comprehensive Cancer Center. "While this analysis is exploratory, intratumoral injection of INT230-6, in which the active drug agents remain in the tumor as demonstrated by this study and cause cancer cell death, appears to have a positive impact on the tumor immune microenvironment and to be a promising approach in metastatic disease alone and in combination."

INT230-6 +/- ipilimumab

Title: *Early Results of Intratumoral INT230-6 Alone or in Combination with Ipilimumab in Subjects with Advanced Sarcomas*
Authors: Ingham, M., et al.
Session: Sarcoma
Session type: Poster Session
Abstract: 11557

As of the April 1, 2021, cutoff, the Phase 1/2 clinical trial evaluated 18 subjects with sarcoma/chordoma on the preliminary efficacy and safety of either INT230-6 alone (n=13) or in combination with the anti-CTLA-4 antibody, ipilimumab (n=5). Patients were treated with and progressed following a median of three prior therapies. INT230-6 was administered intratumorally every two weeks for five doses either alone or with 3 mg/kg of ipilimumab dosed every three weeks for four doses. Preliminary efficacy measured disease control rate (DCR) and median overall survival (mOS). Additional outcome measures included safety/tolerability, response in the injected tumor and the pharmacokinetic profile.

In the overall sarcoma/chordoma population INT230-6 monotherapy and combination subjects showed a disease control rate (DCR) at > 50 days (approximate 2 months assessment) of 60% and an estimated mOS of 23.6 months with 75% of subjects having a Royal Marsden Hospital index (RMHI) score of 2. Based on historical controls, a RMHI score of 2 is associated with an overall survival of between 3 and 6 months in sarcoma (*Oncotarget*, Vol. 7, No 39. July 2016). In addition, there were four INT230-6 monotherapy subjects who showed abscopal effects in multiple deep and distal tumors.

INT230-6, either as monotherapy or in combination with ipilimumab, was well tolerated. The most common adverse events (AEs) were localized tumor-related pain, nausea, fatigue and vomiting. AEs were mild to moderate (24% grade 3) with no Grade 4 or 5 AEs.

“Sarcoma has been a very challenging cancer to treat and has proven resistant to checkpoint blockade. Novel immunotherapy-based approaches are needed, and sarcoma is an attractive cancer for intratumoral injection,” said Matthew Ingham, M.D., Assistant Professor of Medicine in the Division of Hematology and Oncology, Columbia University Irving Medical Center. “Although early, the results from this ongoing study are showing compelling early efficacy with this intratumoral approach as monotherapy, and we look forward to seeing if antigen presentation with this approach will be enhanced by combination with a checkpoint inhibitor.”

To assess drug response the study employed RECIST and then iRECIST, which measure the change in longest diameter of tumors. An increase in diameter of 20% is considered progressive disease. RECIST methodology may not be a good measure of clinical benefit with intratumoral INT230-6 given that drug dosing is based on tumor volume. Evaluation of tumor enlargement is complicated by the amount of INT230-6 injected. During the first two months (5 sessions) of INT230-6 treatment patients could have received an intratumoral dose of drug equivalent from 25 to 250% of their tumor’s volume depending on the cohort. The potential to retain a significant percentage of the fluid prior to the first scan is high. There is also the possibility for immune infiltration, which can also increase tumor size. As a result, overall survival may be a more appropriate endpoint to assess efficacy of this novel treatment modality.

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 that helps disperse the drugs throughout tumors for diffusion into cancer cells.

About Intensity Therapeutics' Clinical Studies

INT230-6 is currently being evaluated in several Phase 2 cohorts (NCT03058289) in patients with various advanced solid tumors as part of Study IT-01. In 2019, the Company signed 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. In 2020, the Company executed 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. In 2021 the Company executed agreements with the Ottawa Hospital Research Institute (OHRI) and the Ontario Institute of Cancer Research (OICR) to study INT230-6 in a randomized controlled neoadjuvant phase 2 study in women with early stage breast cancer (the INVINCIBLE study) (NCT04781725).

About Intensity Therapeutics

Intensity Therapeutics, Inc. is a privately held, 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. The Company executed a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute's (NCI) Vaccine Branch in 2014 partnerships with Merck in 2019, with Bristol-Myers Squibb in 2020 and with OHRI and OICR in 2021. For more information, please visit www.intensitytherapeutics.com and follow us 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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