Oncternal Therapeutics Announces Presentation of Three Posters at AACR 2021 Virtual Meeting

April 12, 2021

- *Updated interim results of a Phase 1b trial of cirmtuzumab and paclitaxel in locally advanced/unresectable or metastatic HER2-negative breast cancer showed 57% of evaluable patients (8 of 14) had a partial response and 29% (4 of 14) had stable disease.*

- *In a preclinical study of cirmtuzumab added to high grade serous ovarian cancer and endometrial cancer cell lines, cirmtuzumab demonstrated both single agent activity and enhanced the anti-proliferative effect of commonly-used chemotherapies.*

- *Preclinical data demonstrated that treatment with Oncternal's investigational selective androgen receptor degraders inhibited androgen receptor-dependent triple negative breast cancer cell and tumor growth.*

SAN DIEGO, April 12, 2021 (GLOBE NEWSWIRE) -- Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies, today announced the presentation of three posters at the American Association for Cancer Research (AACR) 2021 Annual Meeting being held virtually from April 10-15, 2021.

"These data highlight the significant potential of our advanced and differentiated ROR1 platform, where cirmtuzumab has demonstrated promising preclinical and clinical activity across a broad spectrum of cancer indications. The results from the current preclinical studies create additional optionality to pursue future indications, which we are actively evaluating while we advance our Phase 2 cirmtuzumab program in mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL) and advance our earlier-stage CAR-T and CAR-NK cell programs that also target ROR1," said James Breitmeyer, M.D., Ph.D., Oncternal's President and CEO.

Poster Presentations:

- **Session Date and Time:** April 10, 2021 8:30 AM – 11:59 PM ET
- **Session Title:** Stem Cell Biology
- **Poster Title:** A Phase 1b Trial of Cirmtuzumab and Paclitaxel in Locally Advanced/Unresectable or Metastatic Her2 Negative Breast Cancer (Poster #LB255)

- In this Phase 1b investigator-initiated clinical trial from the University of California San Diego (UC San Diego) School of Medicine, 15 patients were treated with cirmtuzumab and paclitaxel after receiving a median of six prior therapies for metastatic disease. Of 15 intent-to-treat patients as of April 10, 2021, eight patients (53%) had a best response of partial response (PR), one of which remained durable for 52 weeks, and four patients (27%) had stable disease (SD). Of the 14 patients who were evaluable for efficacy per protocol, eight patients (57%) had a PR and four patients (29%) had SD. All reported adverse events were related to paclitaxel except for one Grade 3 neutropenia that was categorized as possibly related to cirmtuzumab. No patient stopped cirmtuzumab due to toxicity, no dose reductions of cirmtuzumab were required and no dose limiting toxicities were observed. The authors concluded that as of the cutoff date, cirmtuzumab given with paclitaxel was well-tolerated and demonstrated no added toxicity over what was expected with paclitaxel alone in heavily pre-treated patients with metastatic breast cancer. As of the cutoff date, all pre-treatment breast cancer samples available for analysis expressed ROR1 as assessed by immunohistochemistry. The authors concluded that further clinical evaluation of cirmtuzumab was warranted in patients with breast cancer.

- **Poster Title:** Inhibition of ovarian and endometrial cancer cell proliferation by an anti-ROR1 monoclonal antibody (Poster #1062)
- **Session Title:** Combination Therapies
- **Session Date and Time:** April 10, 2021 8:30 AM – 11:59 PM ET

In this preclinical study from the University of New South Wales, high-grade serous ovarian cancer (HGSOC) and endometrial cancer cell lines were treated with cirmtuzumab alone or in combination with chemotherapeutic agents, cisplatin, paclitaxel, or the PARP inhibitor olaparib. The authors concluded that cirmtuzumab demonstrated single agent activity against these tumor types, and also enhanced the anti-proliferative effects of commonly-used chemotherapies in these cancers. Future studies will further evaluate cirmtuzumab in ovarian and endometrial cancers *in vitro* and in relevant *in vivo* models.

- **Poster Title:** Selective androgen receptor degraders for the treatment of androgen receptor-positive, triple-negative breast cancer (Poster # 1235)
- **Session Title:** Novel Antitumor Agents
- **Session Date and Time:** April 10, 2021 8:30 AM – 11:59 PM ET

In this preclinical study from the University of Tennessee, androgen receptor (AR)-positive triple negative breast cancer (TNBC) cell proliferation and

tumor growth were inhibited using Oncternal's investigational selective androgen receptor degraders (SARDs). Notably, the SARDs demonstrated anti-tumor activity in a TNBC patient-derived xenograft model expressing a splice variant of the AR. Oncternal believes that these results support further development of Oncternal's SARDs as a potential treatment for women affected by the luminal androgen receptor (LAR) subtype of TNBC.

About Cirmtuzumab
Cirmtuzumab is an investigational, potentially first-in-class monoclonal antibody targeting ROR1, or Receptor tyrosine kinase-like Orphan Receptor 1. Cirmtuzumab is currently being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of MCL or CLL, in a collaboration with the University of California San Diego (UC San Diego) School of Medicine and the California Institute for Regenerative Medicine (CIRM). In addition, Oncternal is supporting two investigator-sponsored studies being conducted at the UC San Diego School of Medicine: (i) a Phase 1b clinical trial of cirmtuzumab in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer, and (ii) a Phase 2 clinical trial of cirmtuzumab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL.

ROR1 is a potentially attractive target for cancer therapy because it is an onco-embryonic antigen – not usually expressed on adult cells, and its expression confers a survival and fitness advantage when reactivated and expressed by tumor cells. Researchers at the UC San Diego School of Medicine discovered that targeting a critical epitope on ROR1 was key to specifically targeting ROR1 expressing tumors. This led to the development of cirmtuzumab, that binds this critical epitope of ROR1, which is highly expressed on many different cancers but not on normal tissues. Preclinical data showed that when cirmtuzumab bound to ROR1, it blocked Wnt5a signaling, inhibited tumor cell proliferation, migration and survival, and induced differentiation of the tumor cells. The FDA has granted Orphan Drug Designations to cirmtuzumab for the treatment of MCL and CLL/small lymphocytic lymphoma. Cirmtuzumab is in clinical development and has not been approved by the FDA for any indication.

About SARDs
Oncternal's preclinical Selective Androgen Receptor Degrader (SARD) program is based on inventions by Professors Duane Miller and Ramesh Narayanan from the University of Tennessee Health Science Center (UTHSC) in Memphis, TN. The androgen receptor (AR) is a validated target for the treatment of castration-resistant prostate cancer (CRPC) and there are currently several FDA-approved AR-targeting therapies. However, resistance development occurs, often through mutations or AR splice variants rendering most therapies ineffective. In preclinical studies, Oncternal's investigational SARDs have demonstrated activity against prostate cancer tumors resistant to approved AR-targeting therapies. Oncternal is currently evaluating strategic development options for SARDs as potential therapies for castration-resistant prostate cancer (CRPC) and LAR-TNBC as well as AR-driven non-oncology indications.

About Oncternal Therapeutics
Oncternal Therapeutics is a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies for the treatment of cancers with critical unmet medical need. Oncternal focuses drug development on promising yet untapped biological pathways implicated in cancer generation or progression. The clinical pipeline includes cirmtuzumab, an investigational monoclonal antibody designed to inhibit the ROR1 pathway, a type I tyrosine kinase-like orphan receptor, that is being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib for the treatment of patients with mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL) and in investigator-sponsored, Phase 1b clinical trial in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer, as well as a Phase 2 clinical trial of cirmtuzumab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL. We are also developing a chimeric antigen receptor T cell (CAR-T) therapy that targets ROR1, which is currently in preclinical development as a potential treatment for hematologic cancers and solid tumors. The clinical pipeline also includes TK216, an investigational targeted small-molecule inhibitor of the ETS family of oncoproteins, that is being evaluated in a Phase 1/2 clinical trial for patients with Ewing sarcoma alone and in combination with vincristine chemotherapy. More information is available at www.oncternal.com.

Forward-Looking Information
Oncternal cautions you that statements included in this press release that are not a description of historical facts are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negatives of these terms or other similar expressions. These statements are based on the Company's current beliefs and expectations. Forward looking statements include statements regarding Oncternal's development programs. Forward looking statements are subject to risks and uncertainties inherent in Oncternal's business, which include, but are not limited to the risk that interim results of the ongoing clinical trials and/or preclinical studies of cirmtuzumab and SARDs do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available and other risks described in the Company's prior press releases as well as in public periodic filings with the U.S. Securities & Exchange Commission. All forward-looking statements in this press release are current only as of the date hereof and, except as required by applicable law, Oncternal undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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