Dynavax's SD-101 and 4SC's Domatinostat Demonstrate Synergy and Induce a Systemic Anti-tumor Response in Preclinical Models

April 1, 2019

BERKELEY, Calif. and PLANEGG-MARTINSRIED, Germany, April 01, 2019 (GLOBE NEWSWIRE) -- Dynavax Technologies Corporation (NASDAQ: DVAX) and 4SC AG (FSE Prime Standard: VSC) today announced the combination of 4SC's orally available class I selective HDAC inhibitor domatinostat (4SC-202) with Dynavax's intratumoral TLR9 agonist SD-101 induced a systemic anti-tumoral immune response in tumor mouse models, resulting in the significant decrease in tumor size of both target tumors and distant site metastases.

Combination of SD-101 with domatinostat showed better results than combinations of SD-101 with competing HDAC inhibitors. The triple combination of both compounds with PD-1 blockade (checkpoint inhibition) demonstrated even higher efficacy.

Émilie Degagné, PhD, scientist at Dynavax will present the data in a poster presentation at the American Association for Cancer Research (AACR) meeting, which takes place from 29 March to 3 April 2019 in Atlanta, USA.

Combined mode of actions of SD-101 plus checkpoint inhibitor plus domatinostat

SD-101 is a TLR9 agonist, which was specifically developed for cancer based upon its ability to stimulate both IFN-α production and the maturation of plasmacytoid dendritic cells into tumor antigen presenting cells. This results in increased activation and proliferation of tumor-specific CD8+ T cells which attack distant site non-injected tumors. Domatinostat, acting via epigenetic regulation, renders tumor cells more visible to the immune system and promotes a general immune response against tumor tissue as well as infiltration of T cells into the tumor tissue.

Preclinical data demonstrate that the combination of intra-tumoral SD-101 and systemic domatinostat strongly synergize to induce substantial regression of the primary (injected) tumor, as well as distant site non-injected tumors, including lung metastases. Checkpoint inhibitors, such as anti-PD-1 antibodies further boost the anti-tumor T-cell response, leading to rejection in mice with high metastatic burden. These data indicate that the combination of these three different treatment classes result in induction of a more potent tumor-specific immune response and better recognition and elimination of tumors by immune cells, especially in cancer patients refractory to anti-PD-1 treatment.

"We believe the induction of innate immunity will be instrumental in the future treatment of cancer and are pleased to work with 4SC as they develop differentiated drug candidates to modulate the immune system," **said Eddie Gray, CEO of Dynavax.** "SD-101 has demonstrated significant antitumor effects by direct enhancement of innate immunity and adds meaningful clinical benefit to anti-PD-1 therapy. The addition of domatinostat to this combination shows encouraging results and we look forward to continuing to assess the potential of this combination."

Jason Loveridge, Ph.D., CEO of 4SC, added: "We thank Eddie Gray and his team at Dynavax for performing these highly promising experiments. We are very impressed by the data on the triple-combination of SD-101, domatinostat and PD-1 blockade and believe there is significant potential for novel combinations based on immunotherapeutics such as these to fight cancer, especially in patients who are resistant to or progressing on treatment with prior immunotherapies. Of particular importance to us was the clear demonstration of domatinostat's superiority as compared to competing HDAC inhibitors."

Abstract ID 2259: Tumor abscopal responses induced by the TLR9 agonist, SD-101, are strongly potentiated by a HDAC class I inhibitor, domatinostat.

Date:	1 April 2019
Time:	1:00 PM – 5:00 PM EDT
Session:	PO.CL06.05 - Combination Immunotherapies 1
Location:	Exhibit Hall B, Section 19, Poster Board Number 18

Further information

About SD-101

SD-101, the Company's lead clinical candidate, is a proprietary, second-generation, Toll-like receptor 9 (TLR9) agonist CpG-C class oligodeoxynucleotide. Dynavax is evaluating this intratumoral TLR9 agonist in several clinical studies to assess its safety and activity, including a Phase 2 study in combination with KEYTRUDA® (pembrolizumab), an anti-PD-1 therapy, in patients with advanced melanoma and in patients with head and neck squamous cell cancer, in a clinical collaboration with Merck. Dynavax maintains all commercial rights to SD-101.

About domatinostat (4SC-202)

Domatinostat is an orally administered small molecule Class I selective HDAC inhibitor with a unique mode of action that was designed to strengthen the body's own anti-tumor immune response. Domatinostat also influences the tumor microenvironment facilitating infiltration of immune cells into the tumor and making it more visible to the immune system.

Domatinostat has been investigated in a Phase I study with 24 heavily pretreated patients with several types of advanced hematologic cancers and was well tolerated. Positive signs of anti-tumor efficacy were also observed; with one complete remission (28 months) and one partial responder (8 months).

In addition to its therapeutic potential in cancer monotherapy, 4SC is evaluating domatinostat's capacity as a partner in combination therapies, specifically in the immuno-oncology area. In this respect, 4SC initiated a Phase Ib/II study of domatinostat in combination with the anti-PD-1 checkpoint inhibitor pembrolizumab in patients with advanced-stage melanoma. A second Phase II study of domatinostat in combination with the anti-PD-L1 checkpoint inhibitor avelumab in patients with advanced-stage microsatellite-stable gastrointestinal cancer is conducted by Prof. David Cunningham of The Royal Marsden NHS Foundation Trust (London, UK).

As soon as results from the aforementioned trials will be available, 4SC plans to advance domatinostat into a potentially pivotal study in combination with a checkpoint inhibitor in PD-(L)1 refractory patients with advanced Merkel-cell carcinoma (MCC).

About Dynavax

Dynavax is a fully-integrated biopharmaceutical company focused on leveraging the power of the body's innate and adaptive immune responses through toll-like receptor (TLR) stimulation. Dynavax discovers and develops novel vaccines and immuno-oncology therapeutics. The Company's first commercial product, HEPLISAV-B® [Hepatitis B Vaccine (Recombinant), Adjuvanted], is approved in the U.S. for prevention of infection caused by all known subtypes of hepatitis B virus in adults age 18 years and older. Dynavax's lead immunotherapy product, SD-101, is an investigational cancer immunotherapeutic currently being evaluated in Phase 1/2 studies and its second cancer immunotherapeutic, DV281, is in Phase 1 development. For more information, visit www.dynavax.com.

About 4SC

4SC AG is a clinical-stage biopharmaceutical company developing small-molecule drugs that can target key indications in cancer with high unmet medical needs. 4SC's pipeline is protected by a comprehensive portfolio of patents and currently comprises three key drug candidates in various stages of preclinical and clinical development: resminostat, domatinostat (4SC-202) and 4SC-208.

4SC aims to generate future growth and enhance its enterprise value by entering into partnerships with pharmaceutical and biotech companies and/or the eventual marketing and sales of approved drugs in select territories by 4SC itself.

4SC is headquartered in Planegg-Martinsried near Munich, Germany. The Company had 47 employees as of 31 December 2018 and is listed on the Prime Standard of the Frankfurt Stock Exchange (FSE Prime Standard: VSC; ISIN: DE000A14KL72).

Forward-looking information

Dynavax

This press release contains "forward-looking" statements. Actual results may differ materially from those set forth in this press release due to the risks and uncertainties inherent in our business, including whether we can timely provide adequate clinical supplies; initiation, enrollment and completion of clinical trials of SD-101; whether data from mouse studies and interim and final results of current and future clinical trials will support the initiation or continuation of clinical trials; issues arising in the regulatory process; the ability to successfully develop and commercialize SD-101; and whether or not Dynavax and parties with whom we are collaborating may reach any future agreement on further studies or a more extensive collaboration beyond the clinical trials contemplated under the existing agreements, as well as other risks detailed in the "Risk Factors" section of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 , as well as discussions of potential risks, uncertainties and other important factors in our other filings with the U.S. Securities and Exchange Commission. We undertake no obligation to revise or update information herein to reflect events or circumstances in the future, even if new information becomes available. Information on Dynavax's website at www.dynavax.com is not incorporated by reference in our current periodic reports with the SEC.

4SC

Information set forth in this press release contains forward-looking statements, which involve risks and uncertainties. The forward-looking statements contained herein represent the judgment of 4SC as of the date of this press release. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond 4SC's control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. 4SC expressly disclaims any obligation or undertaking to release any updates or revisions to any such statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based.

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Source: Dynavax Technologies Corporation