Clinical Data Presented from PIVOT-02 Study of Bempegaldesleukin (NKTR-214) with Nivolumab in Metastatic Urothelial Carcinoma Patients at the 2019 ASCO Genitourinary Cancers Symposium

February 15, 2019

Analyst conference call with urothelial cancer specialist to be held at 2:00 p.m. Pacific Time today

SAN FRANCISCO, Feb. 15, 2019 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) announced today a presentation of new clinical data for bempegaldesleukin[1] (NKTR-214) in combination with nivolumab in patients with first-line (1L) advanced or metastatic urothelial carcinoma at the 2019 American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium (GU) in San Francisco, CA.

The preliminary results from patients enrolled in the 1L urothelial cancer cohort in the ongoing PIVOT-02 Phase 1/2 study were shared in a poster presentation today titled, *"NKTR-214 + nivolumab in first-line advanced/metastatic urothelial carcinoma (mUC): Updated results from PIVOT-02"* by Arlene O. Siefker-Radtke, M.D., Professor, Department of Genitourinary Medical Oncology, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center and Clinical Co-Leader of the Bladder Cancer SPORE Executive Committee.

"Preliminary data from the ongoing PIVOT-02 trial in metastatic urothelial cancer patients demonstrated important response rates, including complete responses, in patients who were cisplatin-ineligible or refused standard of care," said Mary Tagliaferri, M.D., Chief Medical Officer of Nektar Therapeutics. "These responses were observed regardless of baseline PD-L1 expression and no relapses occurred. In this cohort of Stage IV bladder cancer patients with a median age of 70, the combination therapy was generally well tolerated with no Grade 4 or 5 adverse events reported. Of note, our translational research demonstrated that in patients with the highest unmet medical need – those whose tumors did not express PD-L1 at their baseline scan – treatment with the combination resulted in 70 percent of patients converting to PD-L1 positive expressors. These data support our development strategy in this tumor setting, including the Phase 2 PIVOT-10 study underway in cisplatin-ineligible urothelial cancer patients with low PD-L1 tumor expression."

Highlights from the ASCO-GU presentation in 1L metastatic urothelial carcinoma patients include:

Clinical Efficacy

Response measured per RECIST 1.1 for per protocol efficacy-evaluable patients treated at the recommended Phase 2 dose (RP2D) and with ≥1 post-treatment scan as of December 3, 2018[2]:

- Best overall response rate (ORR) was 48% (13/27) in efficacy-evaluable patients, with a 19% (5/27) complete response (CR) rate.[3]
- ORR by immune-related RECIST (irRECIST) was 52% (14/27); ORR in patients with visceral non-nodal metastases was 53% (8/15).
- ORR in patients that refused standard of care was 55% (6/11); in cisplatin-ineligible patients ORR was 44% (7/16).
- Disease control rate (DCR) was 70% (defined as CR + partial response (PR) + stable disease (SD)).
- Median percent reduction in target lesions from baseline in all 27 efficacy-evaluable patients was 32%.
- Median percent reduction in target lesions from baseline in all 13 responders was 78%.
- Median time to response was 2.0 months.
- In patients with RECIST response, no patients discontinued due to relapse.
- Amongst the 23 patients with known pre-treatment programmed death-ligand 1 (PD-L1) status, ORR in PD-L1 negative patients was 45% (5/11) and in PD-L1 positive patients was 50% (6/12).

Clinical Safety

- Treatment was generally well tolerated and the most common (>15%) treatment-related adverse events (TRAEs) were flu-like symptoms[4] (71%), fatigue (56%), rash (46%) and pruritus (32%), decreased appetite (27%) and nausea (22%).
- A total of 6/41 (15%) of patients experienced a Grade 3 TRAE, with 4 patients discontinuing due to a TRAE.
- No patients experienced a Grade 4/5 TRAE.

Biomarkers and Mechanism of Action

- 70% (7/10) of patients who were PD-L1 negative at baseline converted to PD-L1 positive by Week 3.
- All patients who were initially PD-L1 positive at baseline remained PD-L1 positive.
- RECIST responses observed were independent of baseline PD-L1 status and CD8+ T cell infiltrate.
- A copy of Dr. Siefker-Radtke's poster presentation of PIVOT-02 data is available on Nektar's corporate website at https://www.nektar.com/download_file/656/0.

The PIVOT-10 study evaluating bempegaldesleukin in combination with nivolumab in 1L locally advanced or metastatic urothelial carcinoma cisplatin-ineligible patients with low PD-L1 expression is currently recruiting patients (NCT03785925).

Analyst Call with Urothelial Cancer Specialist
Nektar will webcast an analyst conference call featuring Dr. Siefker-Radtke today, Friday, February 15, 2019 at 2:00 p.m. Pacific Time. The conference call may be accessed by dialing 877-881-2183 (toll-free) or 970-315-0453 (international) with the conference call passcode 9688945. The webcast and slides for the conference call can be accessed through a link posted on the Investors section of the Nektar website at https://ir.nektar.com/. The webcast of the conference call will be available for replay through March 15, 2019.

About Bempegaldesleukin (NKTR-214)
Bempegaldesleukin is an investigational, first-in-class, CD-122-preferential IL-2 pathway agonist designed to provide rapid activation and proliferation of cancer-killing immune cells, known as CD8+ effector T cells and natural killer (NK) cells, without over activating the immune system. Bempegaldesleukin stimulates these cancer-killing immune cells in the body by targeting CD122 specific receptors found on the surface of these immune cells. CD122, which is also known as the Interleukin-2 receptor beta subunit, is a key signaling receptor that is known to increase proliferation of these effector T cells.[5] In clinical and preclinical studies, treatment with bempegaldesleukin resulted in expansion of these cells and mobilization into the tumor micro-environment.[6,7] Bempegaldesleukin has an antibody-like dosing regimen similar to the existing checkpoint inhibitor class of approved medicines.

About Nektar
Nektar Therapeutics is a research-based development stage biopharmaceutical company whose mission is to discover and develop innovative medicines to address the unmet medical needs of patients. Our R&D pipeline of new investigational medicines includes treatments for cancer, auto-immune disease and chronic pain. We leverage Nektar's proprietary and proven chemistry platform in the discovery and design of our new therapeutic candidates. Nektar is headquartered in San Francisco, California, with additional operations in Huntsville, Alabama and Hyderabad, India. Further information about the company and its drug development programs and capabilities may be found online at www.nektar.com.

Forward-Looking Statements
This press release contains forward-looking statements which can be identified by words such as: "will," "may," "designed" and similar references to future periods. Examples of forward-looking statements include, among others, statements we make regarding the therapeutic potential bempegaldesleukin in combination with other therapeutic agents, and the availability of results and outcomes from our clinical and preclinical studies. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, anticipated events and trends, and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results to differ materially from those indicated in the forward-looking statements include, among others: (i) our statements regarding the therapeutic potential of bempegaldesleukin are based on preclinical and clinical findings and observations to date from ongoing clinical studies; (ii) bempegaldesleukin is in early stage clinical development and the risk of failure remains high and failure can unexpectedly occur at any stage for one or more of the cancer indications being studied prior to regulatory approval due to lack of sufficient efficacy, safety considerations or other factors that negatively impact drug development; (iii) data reported from ongoing clinical trials is necessarily interim data only and the final results will change based on continuing observations from patients that currently remain enrolled in the trials and new observations from patients enrolling in the trials; (iv) scientific discovery of new medical breakthroughs is an inherently uncertain process and the future regulatory approval of potential new drug candidates (such as bempegaldesleukin) is therefore very uncertain and unpredictable; (v) patents may not issue from our patent applications for our drug candidates, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (vi) certain other important risks and uncertainties set forth in Nektar's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 8, 2018. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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[2] Efficacy-evaluable defined per protocol as patients with at least one post-baseline scan. As of 12/3/2018, one patient was excluded for non-eligibility (no target lesion), and three patients discontinued prior to first scan (one due to patient decision; one due to clinical progression; one due to death from disease); ten patients pending first scan in database.

[3] ORR by primary investigator assessment included four unconfirmed responses: two patients with uPR and one patient with uCR pending confirmatory scan and one patient with uPR discontinued for AE after first scan with no confirmatory scan. Since 12/3/2018, three of four patients have had scans confirming responses (including CR).

[4] Flu-like symptoms includes preferred terms: chills, influenza, influenza-like illness, pyrexia

[5] Boyman, J., et al., Nature Reviews Immunology, 2012, 12, 180-190.

[6] Charych, D., et al., Clin Can Res; 22(3) February 1, 2016

[7] Diab, A., et al., Journal for ImmunoTherapy of Cancer 2016, 4(Suppl 1): P369

View original content:http://www.prnewswire.com/news-releases/clinical-data-presented-from-pivot-02-study-of-bempegaldesleukin-nktr-214-with-nivolumab-in-metastatic-urothelial-carcinoma-patients-at-the-2019-asco-genitourinary-cancers-symposium-300796751.html

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