

## News Release

### **NKTR-102 Demonstrates Sustained Clinical Benefit in 46% of Patients with Metastatic Breast Cancer in Data Presented at 2011 American Society of Clinical Oncology Annual Meeting**

***High rate of confirmed response maintained in poor prognosis and heavily pre-treated patients including those with visceral disease***

**Chicago, Illinois and San Francisco, Calif, June 4, 2011** – Nektar Therapeutics (Nasdaq: NKTR) today announced positive results from a Phase 2 clinical study evaluating single-agent NKTR-102 as a second- and third-line treatment in patients with metastatic breast cancer during the 2011 American Society of Clinical Oncology Meeting (ASCO). NKTR-102, a next-generation topoisomerase I inhibitor, is Nektar's lead oncology drug candidate and is being evaluated in multiple cancer indications. The randomized Simon two-stage study presented at ASCO evaluated two 145 mg/m<sup>2</sup> dose schedules of single-agent NKTR-102, every two weeks (q14d) and every three weeks (q21d), in 70 metastatic breast cancer patients who failed a prior taxane therapy. Eighty-nine percent (62/70) of patients in the study received a prior anthracycline/taxane with or without capecitabine.

More than one million women worldwide are diagnosed with breast cancer every year and the disease is the leading cause of cancer-related death among women.<sup>1</sup>

A total of 66 of the 70 patients treated with single-agent NKTR-102 in the Phase 2 study were assessable for the primary endpoint of objective tumor response rate (ORR), including confirmed complete responses (CRs) and partial responses (PRs) per RECIST 1.0. As of May 9, 2011, for the q14d day schedule, the confirmed and unconfirmed ORR was 35 percent (11/31) and the confirmed ORR was 32 percent (10/31), including two confirmed CRs. Clinical benefit rate for the 31 evaluable patients in the q14d schedule was 42% (13/31) (defined as confirmed CR+ PR+ Stable Disease (SD)  $\geq$ 6 mos). For the q21d schedule, the confirmed and unconfirmed ORR was 31 percent (11/35) and the confirmed ORR was 26 percent (9/35).

Clinical benefit rate for the 35 evaluable patients in the q21d schedule was 49% (17/35). Clinical benefit rate for the overall study population was 46%. An additional four patients in the study had near CRs, with 100% disappearance of all target lesions.

“NKTR-102 is emerging as a promising anti-cancer investigational treatment with the potential to become the first topoisomerase I-inhibitor to be used in the fight against breast cancer,” said Prof. Ahmad Awada, Head of the Medical Oncology Clinic at the Institut Jules Bordet in Brussels, Belgium. “The drug’s high confirmed objective response rate and clinical benefit is very interesting, particularly when one observes that this response rate was maintained in patients pre-treated with anthracyclines, taxanes with or without capecitabine, and also maintained in poor prognosis subsets within the study, such as triple-negative breast cancer and patients with visceral disease.”

The confirmed ORR in patients previously treated with anthracycline/taxane/capecitabine was 31% (5/16); confirmed ORR in patients with metastatic triple-negative breast cancer was 39% (7/18); and confirmed ORR in patients with visceral disease was 30% (17/57).

“The every three week dose schedule appears well-tolerated overall and demonstrates encouraging PFS and OS of 5.3 months and 13.1 months, respectively,” continued Dr. Awada. “We are in need of effective new therapeutic options whose mechanism of action is different from those already available for women with metastatic breast cancer and we look forward to NKTR-102 entering Phase 3 development.”

Patients treated in the single-agent NKTR-102 study had a median of two lines of prior cytotoxic treatments for metastatic disease. Seventy-four percent (52/70) of the patients received neoadjuvant and/or adjuvant therapy and 86% (60/70) had visceral disease.

“The clinical benefit we’ve observed in multiple tumor settings with NKTR-102, where a highly active topoisomerase 1 inhibitor could be extremely useful, makes us very excited about the future of this new anticancer drug candidate,” said Lorianne Masuoka, M.D., Senior Vice President and Chief Medical Officer.

Side effects were generally manageable with dose-limiting toxicity consisting primarily of Grade 3 diarrhea (20-23%) typically occurring after three months of therapy for both schedules. Neuropathy and alopecia were minimal with only one patient experiencing G2 alopecia in the

study. Both neuropathy and alopecia are significant adverse events commonly associated with standard breast cancer therapies [Safety Tables, Figures D and E].

### NKTR-102 Phase 2 Data Presentation in Metastatic Breast Cancer

- Awada et. al., *Antitumor activity in a randomized phase II study comparing two schedules of NKTR-102 in patients (Pts) with pretreated metastatic breast cancer (MBC).*

Abstract #1034, Poster Board #24

Poster Discussion Session: Breast Cancer - Triple-negative/Cytotoxics/Local Therapy

Session Date and Time: Saturday, June 4, 2011, 2:00 PM – 6:00 PM, Central Time

Location: E450b

**Figure A: Efficacy Table: Objective Tumor Response Rate by RECIST (Investigator Assessment)**

Response by RECIST v 1.0	NKTR-102 145 mg/m <sup>2</sup> q14d	NKTR-102 145 mg/m <sup>2</sup> q21d	TOTAL
N	31*	35	66
ORR (confirmed + unconfirmed)	11 (35%)	11 (31%)	22 (33%)
ORR (confirmed)	10 (32%)	9 (26%)	19 (29%)
CR (confirmed)	2 (7%)	0	2 (3%)
PR (confirmed)	8 (26%)	9 (26%)	17 (26%)
SD	12 (39%)	16 (46%)	28 (42%)
PD	9 (29%)	10 (29%)	19 (29%)
Median duration of response	8.3 months	4.4 months	5.8 months
Clinical benefit (CR+PR+SD≥6 months)	13 (42%)	17 (49%)	30 (46%)
Median progression-free survival**	3.5 months	5.3 months	4.6 months
Median overall survival**	8.8 months	13.1 months	10.3 months

\*4 patients in the Q14 day arm with no post-baseline scans, but no evidence of progression were excluded from analysis in the evaluable population.

\*\*based on a Kaplan-Meier analysis for the intent-to-treat population.

**Figure B: Efficacy Table: Response rate by prior therapy**

Prior Therapy Subgroup	Response by RECIST v 1.0		
	Evaluable Patients		
	NKTR-102 145 mg/m <sup>2</sup> q14d N=31	NKTR-102 145 mg/m <sup>2</sup> q21d N=35	TOTAL  N=66
Prior A/T only ORR (confirmed)	7/22 (32%)	5/21 (24%)	12/43 (28%)
Prior A/T in MBC ORR (confirmed)	3/7 (43%)	2/9 (22%)	5/16 (31%)
Prior A/T/C ORR (confirmed)	2/6 (33%)	3/10 (30%)	5/16 (31%)

**Figure C: Efficacy Table: Response rate by tumor characteristics**

Disease Subgroup	Response by RECIST v 1.0 Evaluable Patients		
	NKTR-102 145 mg/m <sup>2</sup> q14d N=31	NKTR-102 145 mg/m <sup>2</sup> q21d N=35	TOTAL N=66
ER+ and/or PR+ ORR (confirmed)	8/21 (38%)	4/21 (19%)	12/42 (29%)
Triple-negative breast cancer ORR (confirmed)	2/8 (25%)	5/10 (50%)	7/18 (39%)
Visceral Disease ORR (confirmed)	8/25 (32%)	9/32 (28%)	17/57 (30%)

**Figure D: Safety Table: Safety-Summary of Drug Related AEs**

Most Common Drug-related Grade 3 and 4 Adverse Events > 5% or event of interest N (%)	NKTR-102 145 mg/m <sup>2</sup> q14d N=35		NKTR-102 145 mg/m <sup>2</sup> q21d N=35	
	Grade 3	Grade 4	Grade 3	Grade 4
Diarrhea	6 (17%)	1 (3%)	8 (23%)	0
Neutropenia	2 (6%)	2 (6%)	3 (9%)	1 (3%)
Dehydration	3 (9%)	0	4 (11%)	0
Fatigue	4 (11%)	0	3 (9%)	0
Vomiting	3 (9%)	0	0	0
Anaemia	1 (3%)	0	0	1 (3%)
Asthenia	2 (6%)	0	0	0
Lethargy	2 (6%)	0	0	0
Lymphopenia	1 (3%)	1 (3%)	0	0
Neutropenic sepsis	0	0	1 (3%)	0
Febrile neutropenia	0	0	1 (3%)	0

Note: There were two possible treatment-related deaths: sepsis (q21d) and acute renal failure following diarrhea (q14d).

### Figure E: Safety Table: Other Safety-Neuropathy and Alopecia

No grade 3 or 4 neuropathy was reported.

	NKTR-102 145 mg/m <sup>2</sup> q14d N=35		NKTR-102 145 mg/m <sup>2</sup> q21d N=35	
	Grade 1	Grade 2	Grade 1	Grade 2
Alopecia	6 (20%)	0	3 (9%)	1 (3%)

### About Metastatic Breast Cancer

More than one million women worldwide are diagnosed with breast cancer globally every year<sup>1</sup>. The chance of developing invasive breast cancer at some time in a woman's life is a little less than one in eight (12%). There are approximately 200,000 new cases of breast cancer in the United States and 430,000 in Europe each year.<sup>2</sup> Metastatic breast cancer refers to cancer that has spread from the breast to distant sites in the body.

Anthracyclines and taxanes (AT) are the most active and widely used chemotherapeutic agents for breast cancer, but the increased use of these agents at an early stage of disease often renders tumors resistant to these drugs by the time the disease recurs, thereby reducing the number of treatment options for metastatic disease. Drugs used to treat patients who progress following AT treatment can have response rates as high as 20-30%; however, resistance develops rapidly and new agents with different mechanisms of action, such as topoisomerase I inhibitors, are needed to allow novel ways to overcome the problem of drug resistance.<sup>3</sup> There are currently no FDA-approved topoisomerase I inhibitors to treat breast cancer.

## **About NKTR-102**

Nektar is developing NKTR-102, a next-generation topoisomerase I inhibitor with reduced peak concentrations and a continuous concentration profile. NKTR-102 was invented by Nektar using its advanced polymer conjugate technology platform, and is the first oncology product candidate to leverage Nektar's releasable polymer technology platform.

In addition to the fully-enrolled Phase 2 studies in platinum-refractory/resistant ovarian cancer and metastatic breast cancer, NKTR-102 is also being tested in a separate Phase 2 clinical trial in patients with second-line colorectal cancer and a Phase 1 clinical trial evaluating NKTR-102 in combination with 5-FU therapy. An expansion arm of the Phase 2 study of single-agent NKTR-102 in platinum-refractory/resistant ovarian cancer in women who failed prior Doxil therapy is also currently enrolling. A Phase 3 study of single-agent NKTR-102 is planned in metastatic breast cancer.

## **About Nektar**

Nektar Therapeutics is a biopharmaceutical company developing novel therapeutics based on its PEGylation and advanced polymer conjugation technology platforms. Nektar's technology and drug development expertise have enabled nine approved products in the U.S. or Europe for leading biopharmaceutical company partners, including UCB's Cimzia(R) for Crohn's disease and rheumatoid arthritis, Roche's PEGASYS(R) for hepatitis C and Amgen's Neulasta(R) for neutropenia.

Nektar has created a robust pipeline of potentially high-value therapeutics to address unmet medical needs by leveraging and expanding its technology platforms to improve and enable molecules. In addition to the releasable polymer technology, Nektar is the first company to create a permanent small molecule-polymer conjugate with enhanced oral bioavailability and restricted entry into the CNS. Nektar is currently conducting clinical and preclinical programs in oncology, pain and other therapeutic areas. Nektar has an exclusive worldwide license agreement with AstraZeneca for its oral NKTR-118 program to treat opioid-induced constipation and its NKTR-119 program for the treatment of pain without constipation side effects. NKTR-102 is being evaluated in Phase 2 clinical studies for the treatment of ovarian, breast and colorectal cancers. NKTR-105 is in a Phase 1 clinical study in cancer patients with refractory

solid tumors. Nektar is headquartered in San Francisco, California, with additional R&D operations in Huntsville, Alabama and Hyderabad, India. Further information about the company and its drug development programs and capabilities may be found online at <http://www.nektar.com>.

This press release contains forward-looking statements that reflect Nektar's current views regarding the potential of its technology platform, the potential of NKTR-102 for breast cancer patients, preliminary results from the Phase 2 clinical trial of NKTR-102 in metastatic breast cancer patients, and the potential of certain other drug candidates in Nektar's pipeline. These forward-looking statements involve substantial risks and uncertainties, including but not limited to one or more of the following: (i) NKTR-102 is in mid-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 (i.e. ovarian cancer, breast cancer, and colorectal cancer) due to efficacy, safety or other unpredictable factors even after earlier clinical results have been positive; (ii) the Phase 2 data for NKTR-102 in breast cancer in this press release remain subject to audit and confirmation procedures, and the final results may change materially and adversely after such procedures are completed; (iii) additional important data will be reported by Nektar in the future regarding the Phase 2 NKTR-102 clinical study in metastatic breast cancer including but not limited to final progression-free survival and overall survival and therefore the complete and final results for this study may differ materially and adversely from these preliminary results; (iv) the timing or success of the commencement or end of clinical trials and commercial launch of new drugs may be delayed or unsuccessful due to commercial and funding considerations, regulatory delays, clinical trial design, slower than anticipated patient enrollment, drug manufacturing challenges, changing standards of care, clinical outcomes, or delay or failure in obtaining regulatory approval in one or more important markets; (v) the data from the NKTR-102 Phase 2 clinical study for breast cancer is not necessarily predictive of success in other cancer indications for which NKTR-102 is being studied (i.e. ovarian and colorectal cancers) or future success in Phase 3 clinical development that is currently planned to be conducted in metastatic breast cancer patients; (vi) the data package required and the timing for regulatory approval of a new drug application is very uncertain and difficult to predict due to broad regulatory discretion, changing standards of care, available approved therapies, the size of the completed clinical trials and the statistical significance of the results, the potential need for comparative clinical studies against approved therapies, and other important variables that are not within the control of Nektar; (vii) Nektar's patent applications for its proprietary or

partner product candidates may not issue, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required in the future; (viii) the uncertain outcome of any future intellectual property, commercial or other litigation related to Nektar's proprietary product candidates, including without limitation NKTR-102; and (ix) certain other important risks and uncertainties set forth in Nektar's Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, 2010, filed with the Securities and Exchange Commission on April 29, 2011. Actual results could differ materially from the forward-looking statements contained in this press release. Nektar undertakes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise.

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<sup>1</sup> American Cancer Society, 2007 Global Cancer Facts and Figures Report.

<sup>2</sup> American Cancer Society, 2009 Global Cancer Facts and Figures Report.

<sup>3</sup> Alvaro and Perez, Mayo Clin Proc. 2009; 84(6):533-545